Executive summary

Scope

At request of the Minister of Social Affairs and Employment, the Dutch expert Committee on Occupational Exposure Safety (DECOS), one of the permanent committees of experts of the Health Council, proposes health-based recommended occupational exposure limits for chemical substances in the air in the workplace. These recommendations serve as basis in setting legally binding occupational exposure limits by the minister.

In this advisory report, the committee evaluates the consequences of exposure to fungal alpha-amylase, an enzyme from the fungus Aspergillus oryzae. Workers in bakeries and flour mills may be exposed to this enzyme. The committee’s conclusions are based on scientific papers published before August 2014.

Physical and chemical properties

The enzyme alpha-amylase from the fungus Aspergillus oryzae, is a 478 amino acid glycoprotein. In pure form it is whitish-yellow and a hygroscopic powder. The enzyme catalyses the hydrolysis of long-chain carbohydrates to maltose and glucose. Fungal alpha-amylase extracts are primarily used as a dough improver in the preparation of bakery products.
Exposure

Exposure to airborne fungal alpha-amylase should be monitored as the content of the allergen in inhalable dust, and has mainly been determined in bakeries. Average concentrations in full-shift inhalable air ranged between the detection limit and a few hundred ng/m$^3$, with maxima up to 30 µg/m$^3$. The highest exposures were observed for workers involved in weighing and mixing, and dough handling activities. Because different quantities of dough improver are used for bread and pastry, exposure is also dependent on the type of bakery. During an intervention programme between 2000 and 2007 in the Netherlands, exposure to alpha-amylase decreased in industrial bakeries and flour mills, but increased at ingredient producers.

Kinetics

Exposure to alpha-amylase occurs from dust particles or liquid aerosols. There are no kinetics data specifically relating to enzymes, but they are considered to behave as other particles. The place of deposition in the airway system depends on the size of the particle. In bakeries, fungal alpha-amylase was predominantly present in dust particles with an aerodynamic diameter larger than 5 µm, with over fifty percent associated with particles larger than 9 µm. The majority of these particles are therefore likely to be deposited in the nose, mouth and upper airways.

Effects

Inhalation of fungal alpha-amylase elicits immunological as well as non-immunological responses. Immunological responses lead to sensitisation, which may induce – at continuing exposure – allergic respiratory symptoms, such as asthma, rhinitis, and rhinoconjunctivitis. The respiratory symptoms can also be caused by irritation, a non-immunological response. The only way to distinguish between the two types of responses is to test people on being sensitised to fungal alpha-amylase. The available studies suggest that sensitisation may occur within months after starting of exposure, but it can take several years to develop symptoms.

Most data on the effects of occupational exposure to fungal alpha-amylase are retrieved from studies on bakery workers and flour millers. The number of cases of specific sensitisation among these workers varies between 1 to 30.
percent. For comparison, the number of cases in the general, non-exposed population varies between 1 and 2 percent.

No studies have been performed on other possible adverse health effects in humans, nor were there relevant animal studies reported.

**Evaluation and recommendation**

In deriving a health-based OEL, the committee considered data on sensitisation as the most relevant. Somebody who is sensitised has a high risk in developing allergic reactions at continuing exposure. Because sensitisation is an irreversible effect, the person in question will be sensitised for the rest of his or her life, and at exposure, may show allergic symptoms. In bakeries not only fungal alpha-amylase is used, but also wheat flour and other additives. Also these substances can induce respiratory symptoms, which are not distinguishable from the symptoms described for alpha-amylase exposure. Such a distinguish can be made for sensitisation by using special immunological tests. Further, the committee did not find evidence that respiratory symptoms occur at lower exposure levels than sensitisation. This means that an occupational exposure limit based on data on sensitisation also prevents the development of respiratory symptoms.

In deriving a health-based occupational exposure limit, data are needed on exposure-response relationships. However, in most studies such a relationship was not investigated due to lack of exposure data. In two independent studies an exposure-response relationship was assessed. Both studies were carried out among bakery workers, used airborne enzyme levels as exposure parameter (measured by the same technique), and tested on sensitisation to fungal alpha-amylase. The outcomes differ somewhat, but according to the committee this is explained by normal statistical variation due to differences in the composition of the population under study.

The Committee is of the opinion that for the effect ‘sensitisation’ no threshold level can be assessed. The reason being that in the general (not occupationally exposed) population already cases of sensitisation to fungal alpha-amylase have been reported. That implies that exposure, irrespective the level, gives a risk in developing sensitisation, and that the setting of reference values is warranted. A reference value is a concentration of alpha-amylase in the air, at which occupational exposure leads to a predefined accepted level of risk of allergic airway sensitisation, compared to the background risk in the general, non-exposed population.

Since the two studies show large similarities, the committee decided to combine the data and to use a linear regression model to derive a reference value.
The reference value is based on an additional sensitisation risk of 1 percent. For fungal alpha-amylase, the committee derived a value of 0.9 ng/m$^3$.

**Health-based recommended reference values for sensitisation**

The committee recommends a reference value of 0.9 ng enzyme/m$^3$ for occupational exposure to fungal alpha-amylase, as an eight-hour time-weighted average concentration. At this concentration workers have an additional sensitisation risk for fungal alpha-amylase of 1 percent compared to the background risk in the general population.