



**Ministry of Environment
and Food of Denmark**
Environmental
Protection Agency

Talcum, cosmetic grade (non-fibrous)

Evaluation of health hazards and proposal of a health-based quality criterion for ambient air

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2 General description

The term 'talc' refers to both mineral talc and industrial products that contain mineral talc in proportions that range from about 35% to almost 100% and are marketed under the name talc. Mineral talc is usually platy (non-fibrous) but may also occur as asbestiform fibres. (IARC 2008). It should be noted that asbestiform talc must not be confused with talc that contains asbestos.

Commercial talc is categorised into cosmetic grade, which is free of asbestos, and industrial grade, which contains other minerals including asbestos. (NTP 1993).

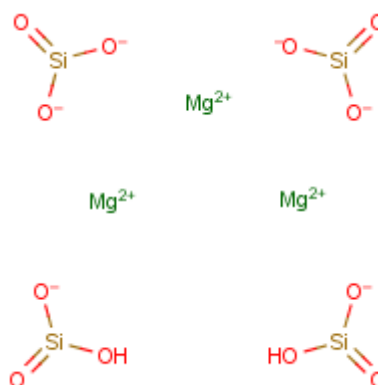
In this evaluation, only the non-fibrous cosmetic grade talc, i.e., non-asbestiform talc in finely powder form is considered in relation to an estimation of a health-based quality criterion for ambient air. The term 'talcum' is used when cosmetic grade talc in finely powder form has been used in a particular study, whereas the term 'talc' is used as a general broad term whenever the references have not stated the grade of the talc used in a particular study.

This document is primarily based on reviews and evaluations prepared by the NTP (1993), IARC (1987a), and IARC (2008).

2.1 Identity

Molecular formula: $\text{Mg}_3\text{H}_2(\text{SiO}_3)_4$

Structural formula:



Molecular weight: 379.26

CAS-no.: 14807-96-6

Synonyms: Cosmetic talc
Hydrous magnesium silicate
Non-asbestiform talc
Non-fibrous talc
Soapstone
Steatite
Talc

2.2 Physical / chemical properties

Description:	Talcum is a fine powder, white to grayish in colour with a greasy feel and lustre.
Purity:	Talc as a pure mineral is composed of 63.5% silicium dioxide, 31.7% magnesium oxide, and 4.8% water.
Melting point:	900-1000 °C
Boiling point:	-
Density:	2.58-2.83 g/ml (at 20°C)
Solubility:	Water: insoluble.
References:	NTP (1993), IARC (1987a).

2.3 Production and use

Talc is a naturally occurring mineral and is produced by mining of talc rocks and processed by crushing, drying, and milling. Contaminating minerals are separated from talcum, which is then finely powdered. (NTP 1993, IARC 1987a).

Technical products of talc are sold in a multitude of grades, which have functional or physical characteristics especially suited for certain applications (IARC 1987a).

Talc is used as a dusting powder (talcum), including baby powder, either alone or with starch or boric acid, for medicinal or toiletry preparations; as an excipient and filler for pills and tablets; and for dusting tablet molds. It is also used as a filler and pigment for paints, putty, and plaster; as a carrier and diluent for pesticides; as an additive to clay in ceramic manufacture; in paper coatings; and for the manufacture of rubber and roofing materials. (NTP 1993).

In Denmark, the total use of talc was approximately 5775 tonnes (data from 2007). Talc was primarily used in paints and varnishes (about 4570 tonnes), fillers (about 590 tonnes), binding agents and adhesives (about 155 tonnes), corrosion inhibitors (about 96 tonnes), reprographic agents (e.f., toners and developers for photocopying (not including photochemicals and fixing agents) about 85 tonnes), non-agricultural pesticides and preservatives (about 42 tonnes), construction materials (about 26 tonnes), and other minor uses in 8 different use categories (about 42 tonnes) (MST 2009).

In Denmark, it is not allowed to produce, import, market, use or work with asbestos or asbestos containing materials (At 2009). These restrictions are also valid for talc containing asbestos.

Talcum is an approved food additive (Positivlisten 2010). It should be noted that there is no distinction between talc and talcum in 'Positivlisten'.

2.4 Environmental occurrence and fate

Mineral talc occurs naturally in many regions of the world where metamorphosed mafic and ultramafic rocks or magnesium carbonates occur. The composition of talc varies widely from one geological deposit to another and even within the same deposit. The main component of talc ore is a crystalline, hydrated silicate of magnesium that is usually in the form of plates (platiform) but may also occur in the form of fibres, asbestiform fibres. Talc ore may contain several other minerals including e.g., calcite, dolomite, magnesite, tremolite, anthophyllite, quartz and serpentines (e.g., chrysotile, the most commonly encountered form of asbestos). There are also deposits that consist almost entirely of platiform talc crystals without significant mixture by other types of crystals or materials. (NTP 1993, IARC 2008, IARC 1987a, ACGIH 2001 – abstract quoted in Toxline).

In its pure form, talc is composed of 63.5% silicium dioxide, 31.7% magnesium oxide, and 4.8% water. Small amounts of aluminium and titanium may substitute to some extent for silicon, and it is common to find iron, nickel, manganese, or chromium substituting to some extent for magnesium. (NTP 1993, IARC 1987a).

2.5 Human exposure

Talc products are sold in a multitude of grades, which have physical or functional characteristics especially suited for particular applications, so occupational and consumer exposures to talc are complex (NTP 1993).

The general population is potentially exposed to cosmetic grade talcum (non-asbestiform talc powder) through its many uses in consumer products, including pharmaceuticals. Based on these uses, human exposure to talcum can occur via inhalation, ingestion, or dermal exposure.

3 Toxicokinetics

3.1 Absorption, distribution, and excretion

3.1.1 Inhalation

Talc particles have been found at autopsy in the lungs of individuals exposed talc (several references quoted in IARC 1987a).

In hamsters, an estimated 6-8% of the inhaled quantity of talc was deposited in the alveoli following a single, 2-hour, nose-only inhalation exposure to talc (high-grade cosmetic talc, consisting of 95% platy talc mineral) at a concentration of 40-75 mg/m³ (median diameter: 6.4-6.9 µm). The biological half-life of the talc deposited in the alveoli was estimated at 7-10 days. No translocation of talc to liver, kidneys, ovaries or other parts of the body was found. (Wehner et al. 1977 – quoted from NTP 1993 and IARC 1987a).

F344/N rats and B6C3F₁ mice were exposed by inhalation to talc at mean exposure concentrations of 2.3, 4.3 or 17 mg/m³ (rats) and 2.2, 5.7 or 20.6 mg/m³ (mice) for 6 hours/day, 5 days/week, for 4 weeks. The resulting lung burdens of talc were 0.08, 0.19 or 0.87 mg/g of lung for rats and 0.1, 0.33 or 1.2 mg/g of lung for mice. (Hanson et al. 1985, Pickrell et al. 1989 – both quoted from NTP 1993).

In rats exposed to talc aerosols (mean respirable dust, 10.8 mg/m³), the mean amounts of talc retained in the lung were 2.5, 4.7 and 12.2 mg per rat following exposures for three, six and 12 months, respectively. These levels were roughly proportional to the cumulative exposures. (Wagner et al. 1977 – quoted from IARC 1987a).

In a life-time study (NTP 1993), F344/N rats (49/50 males per group, 50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6 hours per day, 5 days per week, for up to 113 weeks (males) or up to 122 weeks (females). Lung talc burdens of male and female rats exposed to 6 mg/m³ were similar and increased progressively from 6 to 24 months. Lung talc burdens of females exposed to 18 mg/m³ also increased progressively from 6 to 24 months, while those of males exposed to 18 mg/m³ remained about the same after 18 months. Lung burdens were generally proportional to exposure concentration at each interim evaluation. For further details, see section 4.4.1.

In a life-time study (NTP 1993), B6C3F₁ mice (47-49 males per group, 48-50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6 hours per day, 5 days per week, for up to 104 weeks. Lung talc burdens of mice exposed to 6 mg/m³ were similar between males and females and increased progressively from 6 to 24 months, except for males at 18 months. The lung talc burdens of mice exposed to 18 mg/m³ were also similar between the sexes at each interim evaluation. Although the talc burdens of males and females increased substantially from 6 to 24 months, the values at 12 and 18 months were similar. Generally, lung burdens of mice exposed to 18 mg/m³ were disproportionately

greater than those of mice exposed to 6 mg/m³, suggesting that clearance of talc from the lung was impaired, or impaired to a greater extent, in mice exposed to 18 mg/m³ than in mice exposed to 6 mg/m³. For further details, see section 4.4.1.

3.1.2 Oral intake

Rats, mice, and guinea pigs were administered a single oral dose of ³H-labelled talc. The oral doses were 50 mg/kg bw for rats, 40 mg/kg bw for mice, and 25 mg/kg bw for guinea pigs. For all three species, more than 95% of the dose was excreted in the faeces 3-4 days after dosing, and less than 2% of the radioactivity was recovered in the urine. No radioactivity was detected in the liver or kidneys. (Phillips et al. 1978 – quoted from NTP 1993 and IARC 1987a).

3.1.3 Dermal contact

No data have been located.

4 Human toxicity

4.1 Single dose toxicity

Respiratory distress syndrome, which can be fatal, has been described in children following massive accidental inhalation of talcum powder (several references quoted in IARC 1987a).

Acute bronchitis and bronchiolitis were found in a 22-month-old boy who died following accidental inhalation of talc (Molnar et al. 1962 – quoted from IARC 1987a).

4.2 Irritation

No data have been located.

4.3 Sensitisation

No data have been located.

4.4 Repeated dose toxicity

4.4.1 Inhalation

According to NTP (1993), exposure to industrial grade talc dust causes pulmonary fibrosis, whereas reports on cosmetic grade talc dust are conflicting. In one study, four of seven workers exposed to cosmetic grade talc at concentrations from 0.4-36 mg/m³ for 4-27 years had histological evidence of pulmonary fibrosis at death (Theriault et al. 1974 – quoted from NTP 1993).

The other studies summarised in NTP (1993) are generally case stories on patients or abusers, studies with no exposure concentrations stated, or exposure to talcum was not by inhalation; therefore, these studies will not be further addressed in this evaluation.

According to NTP (1993), inhalation of pure talc is known to result in a disease known as talcosis, which may include acute or chronic bronchitis and interstitial inflammation. Radiographically, the lesion appears as a small, irregular nodule, typical of a small-airway obstruction.

A review of epidemiological studies (Kleinfeld et al. 1992 – abstract from Toxline) revealed that the pulmonary damage induced by exposure to talc or talc containing mixtures has been found to vary depending on the precise composition of the inhaled dust. Clinical symptoms and the pulmonary pathology associated with talc associated lung diseases have been reported to be similar to those of other pneumoconioses. Three groups of microscopic pulmonary lesions have been

identified in talc exposed persons including diffuse interstitial fibrosis with collagen deposition, the presence of nodules containing birefringent particles, and foreign body granulomas. Epidemiological studies on mortality associated with talc inhalation have reached different quantitative conclusions on the pathogenicity of talc. Suggestions for decreasing exposure to talc dust were presented along with recommendations for future research in this area.

Cancer incidence (see Section 3.7.1) and cause-specific mortality were studied in a male cohort of 94 talc miners (northern Norway) who had been employed for at least 1 year during 1944-1972 and 295 talc millers (western Norway) who had been employed for at least 2 years during 1935-1972 (Wergeland et al. 1990). The follow-up was begun at the date of entry into the cohort or 1 January 1953, whichever came latest, and ended at date of death or 31 December 1987, whichever came first.

The majority of the miners and millers could be classified according to the degree of individual dust exposure into three categories (low, medium or high), based on subjective assessment by colleagues; at least 25% of the cohort belonged to the highest exposure category. The level of dust exposure was not registered during the actual exposure period (before 1972), but samples were collected in 1980-1982. Total dust levels varied greatly by job category and workplace (mine: 0.94-97.35 mg/m³; mill: 1.4-54.1 mg/m³), with peak exposures in the mine by drilling (318.9 mg/m³) and in the mill by working in the store house (109 mg/m³). The fibre concentration varied from less than 0.2 up to 0.9 fibres/ml. Dust samples from both the mine and the mill contained less than 1% quartz. The mean concentration of radon daughters in the mine was 3.5 pCi/l (range: 1.5-7.5 pCi/l).

In both the talc miners and the millers, total mortality was lower than expected (SMR 75, 95% CI 62-89, with 117 observed deaths and 155.2 expected). In particular, the mortality from non-malignant respiratory diseases was decreased, with one observed death among miners (2.5 expected) and two observed deaths among millers (8.4 expected); the diagnosis was pneumonia in all three cases. No kind of pneumoconiosis was recorded as the main cause of death.

The authors concluded that the study did not confirm an association between respiratory disease mortality and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied, but that further follow-up time is needed to lessen any impact of “healthy worker” selection.

Wild et al. (2002) studied whether the mortality from non-malignant and malignant (see Section 3.7.1) respiratory diseases of workers employed in French and Austrian talc mines and mills was related to their long-term occupational exposure. Two historical cohorts were set up comprising all male subjects who had been working continuously for at least one year in talc producing companies in France and Austria. The mortality within the cohorts was compared with local death rates. Two nested case-control studies focusing on non-malignant and malignant (see Section 3.7.1) respiratory diseases were set up to estimate possible dose-response relations with cumulative exposure to talc dust based on an industry specific job exposure matrix.

The French cohort (1070 employees) consisted of those employed at a site in the French Pyrenees and working between 1945 and 1994. In talc from this site, the quartz contamination was low (from non-detectable to less than 3%).

The Austrian cohort (542 employees) consisted of the workers employed between 1972 and 1995 in one of three sites in the Austrian Alps. Talc from two of the three sites had a content of quartz that was less than 4%, while that of the third plant had higher but unspecified levels.

Four exposure groups were characterised according to measured and estimated levels of talc dust: 1) No exposure (office workers), 2) $< 5 \text{ mg/m}^3$ (subjects with no direct contact to talc dust), 3) $5\text{-}30 \text{ mg/m}^3$ (all jobs which did not enter one of the other groups), and 4) $> 30 \text{ mg/m}^3$ (past production jobs). Then job histories of cases and controls were converted into cumulative exposure to talc dust by summing the products of duration and level of exposure for each of the tasks held by the subject (y.mg/m^3).

A non-significant excess mortality was found for all non-malignant respiratory diseases in the French cohort due to a significant excess for pneumoconiosis (SMR 5.56, three observed, 95% CI 1.12-16.2). The case-control study of non-malignant respiratory disease showed an increased mortality in the highest exposure groups (odds ratio (OR) 2.5 for a cumulative exposure $>800 \text{ y.mg/m}^3$) with a significant trend (OR/100 y.mg/m^3 1.08) with cumulative exposure to talc. Adjustment on smoking and exposure to quartz did not influence these results to any extent. The authors concluded that the mortality from non-malignant respiratory disease was found to be related to high cumulative exposure to talc dust.

The effects on respiratory health of talc dust, free of asbestiform fibres, at or below airborne concentrations of 2 mg/m^3 were studied in a longitudinal survey of talc workers (Wild et al. 2008). The respiratory health and dust exposure of all workers with at least 5 years of employment at two talc producing facilities in France and Austria were surveyed between 1988 and 2003. The quartz content of the French talc was reported to be below 1%, while the Austrian talc was reported to contain up to 3% quartz.

Standard forced expiratory volumes (1421 spirometries) and standard chest x rays (1153) were obtained on repeated occasions and recorded. Of a target population of 430 subjects (300 from the French facility and 130 from the Austrian facility), 378 (88%) were examined at least twice.

The talc exposure of all jobs had been systematically measured since 1985 at the French site and since 1988 at the Austrian site. A quantitative site-specific job exposure matrix (JEM) for job-time period combinations was set up based on 4602 personal exposure measurements of respirable dust and qualitative descriptions of the industrial processes and individual protection devices.

In the French talc mill, overall exposure decreased from a geometric mean exposure of 1.95 mg/m^3 with a 3.9 geometric standard deviation (GSD) in 1986 (502 measurements) to 0.80 mg/m^3 (GSD 4.3) in 2003 (208 measurements). According to the authors, these high GSDs are mainly due to the very different exposures according to different job codes. Overall, 176 job-time periods were identified. An exposure greater than 5 mg/m^3 was coded for 28 job periods all of which ended before 1992. The highest current JEM levels (3 mg/m^3) were in the granulation workshop and bag filling stations.

In the Austrian talc mill, the geometric mean exposure between 1988 and 1995 was 0.75 mg/m^3 (GSD 3.67, based on 416 measurements) and since 1996 it was 0.30 mg/m^3 (GSD 3.25, based on 237 measurements). The JEM contained 47 job-time period combinations. An exposure higher than 5 mg/m^3 was coded for 13 job periods in a talc company taken over in the late 1980s in which no measurements

had been performed but in which the exposure was described as high. Currently no exposure exceeded 1 mg/m³.

The mean estimated talc dust concentration during the mean duration of follow-up (14.5 years) was 1.46 mg/m³.

Overall, ignoring the exposure, the forced expiratory volume in one second (FEV₁) decreased by 25 ml per year (95% CI -21 to -29). The standardised values (based on expected values according to age, sex and height) decreased with total cumulative exposure (FEV₁ decreased by 6.58 ml per 10 years.mg/m³ of the overall cumulative exposure, 95% CI -13.81 to -0.65), but not with the cumulative exposure since inclusion. Similarly, the prevalence of small radiological opacities was found to increase with the exposure estimation at inclusion, but not with the cumulative exposure since inclusion.

The authors concluded that, although early exposure levels to talc as assessed at inclusion were associated with decreased lung function and an increased prevalence of small radiological opacities, there was no evidence of detrimental effects of talc exposure, as assessed within the study period, on lung function and small radiological opacities.

4.4.2 Oral intake

No data have been located.

4.4.3 Dermal contact

No data have been located.

4.5 Toxicity to reproduction

No data have been located.

4.6 Mutagenic and genotoxic effects

No data have been located.

4.7 Carcinogenic effects

4.7.1 Inhalation

A number of mortality studies have been summarised in IARC (1987a). According to IARC, nearly all measurements of dust exposures made prior to approximately 1970 were done by collecting particles in an impinger and counting them by optical microscopy. Concentrations were thus expressed as millions of particles per cubic foot of air (mppcf).

Two studies have been reported on New York talc miners and millers (Kleinfeld et al. 1967, 1974 – quoted from IARC 1987a). According to IARC, the results of the studies are substantially the same and only the more complete 1974 results were reported in the IARC (1987a) monograph. Men employed in 1940 who had accumulated 15 or more years of exposure to commercial talc dust (containing

tremolite and anthophyllite (asbestiform and non-asbestiform talc), carbonate dusts and a small amount of free silica) as well as those who achieved a minimum of 15 years of such exposure between 1940 and 1969, were included in the study (in total 260 workers). Dust counts were provided for the years 1966-1969: mines had median counts ranging from 9-19 mppcf, and mills 20-24 mppcf; dust counts and fibre counts reported for the year 1972 ranged from 3-7 mppcf and 2-3 fibres/cm³ in mines and 7-28 mppcf and 24-62 fibres/cm³ in mills. Proportionate mortality was calculated utilising US white male mortality for the year 1955, the median year of the 108 deaths observed. Mortality from lung and pleural cancer showed a three-fold overall increase (12% observed, 3.7% expected). No significant excess for gastrointestinal cancers was found. One peritoneal mesothelioma was noted. The IARC Working Group noted that no data were available on smoking or on cumulative dose in individual workers, nor were further data given about the distribution of workers among the several mines and mills from which the records were extracted.

A cohort mortality study has been conducted of 398 white men initially employed between 1947 and 1959 in mining and milling talc in the New York State, St Lawrence County (Brown et al. 1979 – quoted from IARC 1987a). In addition to talc, the product contained tremolite, anthophyllite and serpentine minerals, some of which were asbestiform. Vital status was ascertained as of 1975. Fifty percent of the workers had been employed less than one year and 27% for ten years or more. Statistically significant excesses in mortality were observed for all malignant neoplasms (19 observed, 10.6 expected; SMR 180), for neoplasms of the respiratory system (10 observed, 3.5 expected; SMR 290), for bronchogenic cancer (9 observed, 3.3 expected; SMR 270), and for all non-malignant respiratory disease (8 observed, 2.9 expected; SMR 277). Evidence of an exposure-response relationship was observed by latency for bronchogenic cancer. The authors concluded that tremolite and anthophyllite were the prime suspected ethiological factors associated with the observed increase in bronchogenic cancer and non-malignant disease. The IARC Working Group noted that no data on smoking were available and that a possible confounding factor was previous exposures at other mines in the area, but exposures to amphibole fibre in all these regional talc operations were reported to be substantially the same.

Time-weighted-average (TWA) exposures to respirable dust and airborne fibres in the mine and mill were reported by Dement et al. (1980 – quoted from IARC 1987a). TWA exposures to respirable dust ranged from 0.23-1.29 mg/m³ in the mine and 0.25-2.95 mg/m³ in the mill. Due to the low free silica content on this talc, exposure to respirable free silica did not exceed 0.025 mg/m³ in the mine and 0.028 mg/m³ in the mill. Airborne fibre levels measured by optical microscopy gave mean exposures in the mine and mill of 4.5 and 5.0 fibres > 5 µm/cm³, respectively, with peak values as high as 29.1 fibres/cm³ in the mill. Further analyses of the airborne fibre samples by electron microscopy showed that 65% of the fibres greater than 5 µm in length were anthophyllite and 7% were tremolite.

A cohort study (Stille and Tabershaw 1982 – quoted from IARC 1987a) has been conducted on the same mine and mill studies by Brown et al. (1979), see previous study. The composition of the cohort was somewhat different as the current study included 655 employees who had ever worked for the company between 1948 and 1977, after exclusion of 35 women office workers and 53 workers for which significant data were not available. Cause-specific mortality rates were based on 113 deaths as of December 1978. The SMR for all sites of cancer was 122 (25 observed, 20.5 expected); 11 cases were respiratory cancers, and 10 of those were lung cancer with SMRs of 163 and 157, respectively. The cohort was then divided according to whether an individual had been employed elsewhere before coming to

work at the particular mine and mill under investigation. Those who had worked only at the company in question (few) were found to have very low mortality from lung cancer (2 observed, 2.6 expected). The IARC Working Group noted a number of methodological problems, including selection bias, lack of statistical testing, small numbers of person-years of exposure, and no analysis with respect to exposure.

In an Italian study (Rubino et al. 1976 – quoted from IARC 1987a), 1514 miners and 478 millers employed for at least one year between 1921 and 1950 in talc mines and mills were studied. The talc was described as quite pure with only some tremolite micro inclusions; no other fibrous mineral was reportedly found. Prior to 1950, exposures were reported to be to approximately 800 mppcf in the mines and to 25 mppcf in the mills; exposures in both areas were reduced to less than 10 mppcf after 1965. Significant increases in specific cause of death among miners were found for silicosis (62 observed, 30.9 expected) and for silico-tuberculosis (18 observed, 9.1 expected). Significant deficits in cause-specific mortality were reported for malignant neoplasms (100 observed, 129.5 expected), malignant neoplasms of the lung, bronchus and trachea (9 observed, 19.7 expected), and malignant neoplasms at other sites (23 observed, 39.9 expected). Two cases of pleural mesothelioma and a high occurrence of silicosis and silico-tuberculosis were found in the comparison group. The IARC Working Group noted that the method used to derive the number of expected deaths was not adequately described, and it was considered that the lack of comparability between the worker and comparison groups could be the main explanation for the mortality increases and deficits observed.

A study of talc exposures in five companies in three regions of Vermont, USA, has been carried out (Selevan et al. 1979 – quoted from IARC 1987a). Analysis of the talc revealed no asbestos and levels of free silica were below 0.25%. The cohort consisted of all white male talc workers who had been radiographed as part of annual voluntary surveys of the Vermont Health Department, who were employed in the Vermont talc industry between 190 and 1969, and who had worked in the industry for at least one year. There were 90 deaths among the 392 members of the cohort. For non-malignant respiratory disease and respiratory cancer, Vermont rates were used for comparison, because they were higher than national rates; for other causes of death, US rates were used. Some increase was noted for malignant neoplasms, and specifically for respiratory neoplasms (6 observed, 3.69 expected), but the increase was not significant. The excess respiratory cancer occurred only among miners (5 observed, 1.15 expected, $p < 0.05$), and the significant excess for non-malignant respiratory disease occurred only among millers (7 observed, 1.72 expected, $p < 0.01$). Most of those dying with non-malignant respiratory disease had radiographic evidence of pneumoconiosis (rounded opacities). Miners were also exposed to radon daughters at mean levels ranging up to 0.12 working levels, with single peaks of 1.0 working level. The IARC Working Group noted that no data on smoking were available, that because of the voluntary nature of the survey the cohort may not have been representative, the unconventional analytical approach, and that the results were not analysed by latency.

Concentrations of respirable dust in mass samples from three Vermont talc mines and mills surveyed in 1975-1976 have been reported by Boundy et al. (1979). Geometric mean exposures to respirable dust ranged from 0.5-5.1 mg/m³ in the mines and from 0.5-2.9 mg/m³ in the mills; however, exposures in the mills were generally higher than those in the mines. Optical fibre counts of up to 60 fibres/cm³ were reported. Analyses showed that talc and magnesite were the major (20-100%) mineral components, chlorite and dolomite minor (5-20%) components.

In a short communication, the mortality of talc workers in Luzenac, France was reported (Léophonte et al. 1983 – quoted from IARC 1987a). The talc in this region is said to contain no asbestos and levels of quartz varying from 0.5 to 3%. The cohort comprised those who left employment between 1 January 1945 and 31 December 1981 having worked for at least one year. Of 470 workers available for study, 256 were living, 209 had died and five were lost due to follow-up; 192/204 with known occupational exposure had worked only at Luzenac. When compared with the regional population, the median age of death was not found to be influenced by dust exposure. There was no significant excess in cancer mortality in general, and, specifically, mortality from respiratory and digestive cancers was not increased. A significant increase in mortality was found for non-malignant respiratory disease, especially for pneumoconiosis and obstructive lung disease. The IARC Working Group noted the unconventional definition of the cohort, that no data on smoking habits were available, and that causes of death were obtained from cases from local doctors, hospitals or families but for controls from regional or national records.

Cancer incidence and cause-specific mortality were studied in a male cohort of 94 talc miners and 295 talc millers (Wergeland et al. 1990).

A higher than expected number of cases occurred for all cancers combined in the mine (15 observed, 10.72 expected), but not in the mill (31 observed, 40.60 expected). The excess number of cases in the mine was confined to cancer of the stomach (3 observed, 1.19 expected), prostate (4 observed, 1.96 expected) and lung (2 observed, 1.27 expected). In the mill, four cases of lung cancer was observed (5.22 expected). In the subgroup of 80 workers who belonged to the highest exposure category, a total of six cases of cancer were observed (13.55 expected); there were no cases of cancer of the lung in this subgroup.

The authors concluded that the study did not confirm an association between lung cancer morbidity and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied. Further follow-up time is needed to lessen any impact of “healthy worker” selection.

Details of the cohort as well as the results regarding mortality from non-malignant respiratory diseases are described in Section 3.4.1.

Wild et al. (2002) studied whether the mortality from non-malignant and malignant respiratory diseases of workers employed in French and Austrian talc mines and mills was related to their long-term occupational exposure. Mortality from lung cancer was in small excess in both cohorts (France, SMR 1.23, 21 cases observed, 95% CI 0.76-1.89; Austria, SMR 1.06, seven cases observed, 95% CI 0.43-2.19). No increasing trend with cumulative exposure to talc could be found in the case control study of lung cancer. Adjustment on smoking and exposure to quartz did not influence these results to any extent. The authors concluded that the small excess in lung cancer does not seem to be attributable to talc.

Details of the cohorts as well as the results regarding mortality from non-malignant respiratory diseases are described in Section 3.4.1.

A cohort study of pottery workers exposed to silica and talc showed an excess risk of lung cancer (SMR 143; 52 observed, 36.3 expected). The increased lung cancer incidence was highest among workers who were simultaneously exposed to silica and non-fibrous talc (SMR 254; 21 observed, 8.3 expected; $p < 0.05$) compared to workers exposed to silica without talc exposure (SMR 137; 18 observed, 13.2 expected; $p > 0.05$). Mortality from lung cancer increased with duration of

exposure to talc (SMR 364 for those with > 15 years of exposure), but not with duration of exposure to silica. (Thomas and Stewart 1987 – quoted from IARC 1987b and NTP 1993).

Non-asbestiform talc has recently been reviewed by IARC (IARC 2008); however, the monograph is not yet published except for the sections ‘Summary of data reported’ and ‘Evaluation’. Below is an extract of the summary:

Workers are exposed to talc during its mining and milling. Reported exposure levels to respirable dust are typically in the range of 1-5 mg/m³ (geometric mean).

The carcinogenic effect of exposure to talc not contaminated by asbestiform fibres has been investigated in five independent but relatively small cohort studies of talc miners and millers in the USA, Norway, Italy, France and Austria. The miners and to a lesser extent the millers in these cohorts were also exposed to quartz. In the miners in the US study, an excess risk for lung cancer was found, which may have been due to exposure to radon daughters and quartz in the workplace. In all the other groups of workers studied, there was no increased risk for lung cancer. In the two studies from Norway and Italy, which included an estimate of cumulative exposure to talc dust, the risk for lung cancer in the highest category was found to be close to or below unity. In a case-control study nested in the combined cohorts of talc workers from France and Austria, there was no tendency of higher risks for lung cancer by increasing cumulative exposure of workers to talc dust. In four of five studies, it was explicitly stated that no case of mesothelioma was observed. In female workers in the Norwegian pulp and paper industry, there was an increased risk for ovarian cancer, which, however, was attributed to exposure to asbestos.

A literature survey (Wild 2006) involved all epidemiological cancer studies mentioning talc as a risk factor. The talc exposed populations were divided into three groups: (1) populations in which no other occupational carcinogen was mentioned (only talc millers satisfied this criterion); (2) populations of talc miners exposed to talc, quartz, and/or radon; and (3) other industrial populations in which talc is associated with quartz, nitrosamines, and asbestos depending on the study. No excess lung cancer mortality was found for talc millers exposed to high levels of talc but without any other potential carcinogen (SMR = 0.92, 42 cases), while the mortality of talc miners exposed to quartz and/or radon was in excess (fixed effect SMR = 1.20; random effect, relative risk RR = 1.85, 40 cases). Six studies in other industrial settings were identified. All reported increased lung cancer mortality among talc exposed workers but the talc exposure was confounded with other carcinogens and only one study was able to adjust on them. In conclusion, no increased lung cancer mortality was observed among talc millers despite their high exposure experience. In populations in which talc was associated with other potential carcinogens, some lung cancer excesses were observed.

4.7.2 Oral intake

Talc particles were found in stomach tumours from Japanese men, possibly due to ingestion of talc-treated rice (Henderson et al. 1975 – quoted from IARC 1987a).

4.7.3 Dermal contact

No data have been located.

5 Animal toxicity

5.1 Single dose toxicity

No data have been located.

5.2 Irritation

No data have been located.

5.3 Sensitisation

No data have been located.

5.4 Repeated dose toxicity

5.4.1 Inhalation

Deaths occurred among rats exposed to a very dense atmosphere of talc (particle size $< 5 \mu\text{m}$) 3 hours a day, for 12 days (Policard 1940 – quoted from NTP 1993 and IARC 1987a). According to NTP (1993), the concentration of talc in the atmosphere was not known and the observed mortality may have been due to suffocation.

Rats exposed to talc by inhalation of 10.8 mg/m^3 (particle size $25 \mu\text{m}$) for 3 months showed minimal lung fibrosis, and no change in severity occurred during the post-exposure period. When rats were exposed to the same atmosphere for a year, minimal to slight fibrosis was observed, and the severity had increased to moderate within a year after cessation of exposure. (Wagner et al. 1977 – quoted from NTP 1993 and IARC 1987a). Neoplastic findings are described in section 4.7.1.

Rats exposed to talc – ‘industrial’ or ‘pharmaceutical’ – at concentrations from $30\text{--}383 \text{ mg/m}^3$ for 9 months developed chronic inflammatory changes, including thickening of the pulmonary artery walls and emphysema (Bethge-Iwanska 1971 – quoted from NTP 1993 and IARC 1987a).

No effect on survival and no histopathological changes were noted in the lung, heart, liver, kidney, or uterus of hamsters exposed to respirable aerosols containing 8 mg/m^3 of cosmetic grade talc for 150 minutes a day, 5 days per week, for 300 days (Wehner 1980 – quoted from NTP 1993 and IARC 1987a). Neoplastic findings are described in section 4.7.1.

In a life-time study, F344/N rats (49/50 males per group, 50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m^3 talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6 hours per day, 5 days per week, until mortality in any exposure group reached 80% (113 weeks for males and

122 weeks for females). These exposure concentrations provided a dose equivalent of 0, 2.8, or 8.4 mg/kg bw/day for male rats and 0, 3.2, or 9.6 mg/kg bw/day for female rats. In a special study, additional groups of rats (22 of each sex per group) were similarly exposed and examined for interim pathology evaluations or pulmonary function tests after 6, 11, 18, and 24 months, and lung biochemistry and cytology studies after 24 months. (NTP 1993).

The talc aerosols had an average mass median aerodynamic diameter of 2.7 μm in the 6 mg/m^3 chamber and a median diameter of 3.2 μm in the 18 mg/m^3 chamber, with geometric standard deviations of 1.9 μm . However, there was a 7-week period beginning at study week 11 during which the chamber concentration for the 18 mg/m^3 rats varied from approximately 30 to 40 mg/m^3 and a 12-week period beginning at approximately week 70 during which there were difficulties in generating the talc aerosol, and the chamber concentrations were substantially lower than the target concentrations.

The exposure concentrations were selected based on a 4-week inhalation study to determine lung talc burden and histopathological changes associated with talc exposure. This study indicated that the amount of talc retained in the lung was similar between sexes and proportional to exposure concentrations. Microscopic examination of the lungs revealed an accumulation of alveolar macrophages in the lungs at the highest exposure concentration (18 mg/m^3). Based on these findings, it was considered that aerosol concentrations greater than 18 mg/m^3 would overwhelm lung clearance mechanisms, impair lung function, and possibly shorten survival.

In the life-time study, survival of male and female rats exposed to talc was similar to that of the controls (9/11, 14/13, 16/9 males/females at 0, 6, 18 mg/m^3 , respectively). Mean body weights of rats exposed to 18 mg/m^3 were slightly lower than those of controls (4 and 14% for males and females, respectively, compared to the control group) after week 65. No treatment-related clinical findings were noted. Absolute and relative lung weights were significantly greater than those of controls from 6 months of exposure (males) or 11 months of exposure (females) at 18 mg/m^3 , and in females at the end of the study at 6 mg/m^3 .

At the microscopic examination, a spectrum of inflammatory, reparative, and proliferative processes in the lungs was noted, see Table 1. Granulomatous inflammation occurred in nearly all exposed rats and the severity increased with exposure duration and concentration. Hyperplasia of the alveolar epithelium and interstitial fibrosis occurred in or near foci of inflammation in many exposed rats, while squamous metaplasia of the alveolar epithelium and squamous cysts were also occasionally seen. Accumulations of macrophages (histiocytes), most containing talc particles, were found in the peribronchial lymphoid tissue of the lung and in the bronchial and mediastinal lymph nodes. Minor alterations attributed to talc exposure were also observed in the upper respiratory tract. Hyperplasia of the respiratory epithelium of the nasal mucosa in males and accumulation of cytoplasmic, eosinophilic droplets in the nasal mucosal epithelium in male and female rats occurred with a concentration-related increased incidence in the exposed groups. Pulmonary lesions were generally similar at the interim evaluations and the end of the study, but varied in incidence, extent and severity with exposure concentration and duration. Neoplastic findings are described in section 4.7.1.

In exposed male and female rats there was a concentration-related impairment of respiratory function, which increased in severity with increasing exposure duration. The impairment was characterized by reductions in lung volume (total lung capacity, vital capacity, and forced vital capacity), lung compliance, gas exchange efficiency (carbon monoxide diffusing capacity), and non-uniform intrapulmonary gas distribution.

Evaluation of lung biochemistry and cytology parameters examined in the bronchoalveolar lavage fluid showed increases in enzymes, total protein, and leukocytes consistent with the morphological findings of a chronic active inflammatory process and cellular degenerative changes. Neither the viability nor the phagocytic activity of alveolar macrophages was significantly affected by exposure to talc. Total lung collagen in the bronchoalveolar lavage fluid was significantly increased in rats at both exposure concentrations after 24 months, while collagenous peptides in lavage fluid and the percentages of newly synthesised protein from females, but not males, were also significantly increased at the 6 or 18 mg/m³ levels. In addition, lung acid proteinase activity was significantly greater in exposed males and females. Rats exposed to talc also had significant increases in collagenous peptides and acid proteinase in lung homogenates.

Table 1. Incidences of selected lung lesions in rats in the lifetime inhalation study of talc (adapted from NTP (1993)).

	Male			Female		
	0 mg/m ³	6 mg/m ³	18 mg/m ³	0 mg/m ³	6 mg/m ³	18 mg/m ³
Lung ^a	49	50	50	50	48	50
Inflammation, granulomatous ^b	2 (1,0) ^c	50** (1.6)	49** (2.3)	2 (1.5)	47** (1.5)	50** (2.8)
Peribronchial hyperplasia, histiocytic	0	12** (1.3)	8** (1.9)	0	8** (1.3)	9** (1.3)
Alveolar epithelium, hyperplasia	5 (2,0)	26** (1.3)	38** (1.7)	2 (1.0)	27** (1.2)	47** (2.1)
Alveolus, metaplasia, squamous	0	0	2 (1.0)	0	0	8** (1.1)
Interstitial, fibrosis, focal	1 (1,0)	16** (1.2)	33** (1.8)	1 (1.0)	24** (1.5)	45** (2.1)
Cyst (squamous)	0	0	3	0	1	7**

** Significantly different ($p \leq 0.01$) from the control by logistic regression

a Number of animals with lung examined microscopically

b Number of animals with lesions

c Average severity grades of lesions in affected animals: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked

In a life-time study, B6C3F1 mice (47-49 males per group, 48-50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6 hours per day, 5 days per week, for up to 104 weeks. These exposure concentrations provided a dose equivalent of 0, 2, or 6 mg/kg bw/day for male mice and 0, 1.3, or 3.9 mg/kg bw/day for female mice. In a special study, additional groups of mice (39-40 of each sex per group) were similarly exposed and examined for interim pathology evaluations, and lung biochemistry and cytology studies after 6, 12, and 18 months of exposure. (NTP 1993).

The talc aerosols had an average mass median aerodynamic diameter of 3.3 μm with a geometric standard deviation of 1.9 μm in the 6 mg/m^3 chamber, and a median diameter of 3.6 μm with a geometric standard deviation of 2.0 μm in the 18 mg/m^3 chamber. However, there was a 12-week period beginning at approximately week 70 during which there were difficulties in generating the talc aerosol, and the chamber concentrations were substantially lower than the target concentrations.

The exposure concentrations were selected based on a 4-week inhalation study to determine lung talc burden and histopathological changes associated with talc exposure. This study indicated that the amount of talc retained in the lung was similar between sexes and proportional to exposure concentrations. Microscopic examination of the lungs revealed an accumulation of alveolar macrophages in the lungs only 18 mg/m^3 . Based on these findings, it was considered that aerosol concentrations greater than 18 mg/m^3 would overwhelm lung clearance mechanisms, impair lung function, and possibly shorten survival.

Survival (30/30, 28/23, 32/25 males/females at 0, 6, 18 mg/m^3 , respectively) and final mean body weights of male and female mice exposed to talc were similar to those of the controls. No treatment-related clinical findings were noted. Absolute and relative lung weights were significantly greater than those of controls at 12 months and at the end of exposure at 18 mg/m^3 , and in females at 18 months at 18 mg/m^3 .

The microscopic examination of the lungs revealed that inhalation exposure of mice to talc was associated with chronic active inflammation and the accumulation of macrophages in the lung, see Table 2. In contrast to rats, hyperplasia of the alveolar epithelium, squamous metaplasia, or interstitial fibrosis was not associated with the inflammatory response in mice. Accumulations of macrophages (histiocytes) containing talc particles were also present in the bronchial lymph node. In the upper respiratory tract, cytoplasmic alteration, consisting of the accumulation of cytoplasmic eosinophilic droplets in the nasal mucosal epithelium, occurred with a concentration-related increased incidence in exposed male and female mice. Neoplastic findings are described in section 4.7.1.

Evaluation of lung biochemistry and cytology parameters examined in the bronchoalveolar lavage fluid showed increases in total protein, beta-glucuronidase, lactate dehydrogenase, glutathione reductase, total nucleated cells, and polymorphonuclear leukocytes in bronchoalveolar lavage fluid were observed primarily in mice exposed to 18 mg/m^3 , although some parameters were also increased in mice exposed to 6 mg/m^3 . The amount of collagenous peptides in lavage fluid and total lung collagen were increased in male and female mice exposed to 18 mg/m^3 . Acid proteinase activity of lung homogenate supernatant fluid was also significantly increased in mice at the 18 mg/m^3 exposure concentration.

Table 2. Incidences of selected lung lesions in mice in the lifetime inhalation study of talc (adapted from NTP (1993)).

	Male			Female		
	0 mg/m ³	6 mg/m ³	18 mg/m ³	0 mg/m ³	6 mg/m ³	18 mg/m ³
Lung ^a	4	47	48	46	48	50
Hyperplasia, macrophage ^b	3 (2.3) ^c	46** (1.4)	48** (2.8)	2 (2.5)	45** (1.6)	43** (2.8)
Inflammation, chronic active	0	16** (1.1)	40** (2.2)	0	25** (1.4)	38** (1.3)
Alveolar epithelium, hyperplasia	1 (1.6)	0	0	0	0	1 (1.0)

** Significantly different ($p \leq 0.01$) from the control by logistic regression

a Number of animals with lung examined microscopically

b Number of animals with lesions

c Average severity grades of lesions in affected animals: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked

5.4.2 Oral intake

No significant decrease in mean life span and no pathological effects were noted in rats fed 100 mg talc for 101 days (Wagner et al. 1977 – quoted from NTP 1993 and IARC 1987a). Neoplastic findings are described in section 4.7.1.

5.4.3 Dermal contact

No data have been located.

5.5 Toxicity to reproduction

5.5.1 Inhalation

No data have been located.

5.5.2 Oral intake

No teratogenic effects were observed in rats, mice, rabbits or hamsters after oral administration of talc. The doses used were 1600 mg/kg bw/day for rats and mice on gestation days 6-15, 900 mg/kg bw/day for rabbits on gestation days 6-18, and 1200 mg/kg bw/day for hamsters on gestation days 6-10 (Food and Drug Research Laboratories 1973 – quoted from NTP 1993 and IARC 1987a).

5.5.3 Dermal contact

No data have been located.

5.6 Mutagenic and genotoxic effects

5.6.1 *In vitro* studies

Talc did not induce mutations in *Salmonella typhimurium* strains TA1530 or HisG46, or in *Saccharomyces cerevisiae* (Litton Bionetics 1974 – quoted from IARC 1987a).

Chromosomal aberrations were not induced in human fibroblasts treated with talc *in vitro* (Litton Bionetics 1974 – quoted from IARC 1987a).

5.6.2 *In vivo* studies

Neither chromosomal aberrations in bone marrow cells nor dominant lethal mutations in germinal cell were induced in rats following oral administration of 30-50000 mg/kg bw talc (Litton Bionetics 1974 – quoted from IARC 1987a).

5.7 Carcinogenic effects

5.7.1 Inhalation

Wistar rats (24 of each sex) was exposed by inhalation to a mean respirable dust concentration of 10.8 mg/m³ (Italian talc containing 92% talc, 3% chlorite, 1% carbonate minerals and 0.5-1% quartz, mean particle size 25 µm) for 7.5 hours per day on five days a week for six (24 rats) or 12 (24 rats) months (Wagner et al. 1977 – quoted from IARC 1987a). Ten days after the end of each exposure period, six rats in each group were killed; a further four rats were killed in each group one year later. Within 28 months of the start of the study, a further 12 animals in each group had died. No lung tumour was observed in rats exposed for six months, while one lung adenoma occurred among those exposed for 12 months. Non-neoplastic findings are described in section 4.4.1. The IARC Working Group noted the limited number of animals allowed to survive longer than 12 months after the end of each exposure period.

In a life-time study (NTP 1993), F344/N rats (49/50 males per group, 50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6 hours per day, 5 days per week, for up to 113 weeks (males) or up to 122 weeks (females). The talc aerosols had an average mass median aerodynamic diameter of 2.7 µm in the 6 mg/m³ chamber and a median diameter of 3.2 µm in the 18 mg/m³ chamber, with geometric standard deviations of 1.9 µm. Survival of male and female rats exposed to talc was similar to that of the controls (9/11, 14/13, 16/9 males/females at 0, 6, 18 mg/m³, respectively). In female rats, the incidences of alveolar/bronchiolar adenoma, carcinoma, and adenoma or carcinoma (combined) in the 18 mg/m³ group were significantly greater than those of controls. The incidences of pulmonary neoplasms in exposed male rats were similar to those in controls. Adrenal medulla pheochromocytomas (benign, malignant, or complex (combined)) occurred with a significant positive trend in male and female rats, and the incidences in the 18 mg/m³ groups were significantly greater than those of controls. Non-neoplastic findings are described in section 4.4.1.

In a life-time study (NTP 1993), B6C3F1 mice (47-49 males per group, 48-50 females per group) were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation (whole-body) for 6

hours per day, 5 days per week, for up to 104 weeks. The talc aerosols had an average mass median aerodynamic diameter of 3.3 μm with a geometric standard deviation of 1.9 μm in the 6 mg/m^3 chamber, and a median diameter of 3.6 μm with a geometric standard deviation of 2.0 μm in the 18 mg/m^3 chamber. Survival of male and female mice exposed to talc were similar to those of the controls (30/30, 28/23, 32/259 males/females at 0, 6, 18 mg/m^3 , respectively). The incidences of pulmonary neoplasms in exposed and control groups of mice were similar. Non-neoplastic findings are described in section 4.4.1.

Under the conditions of the inhalation studies in rats and mice, the NTP (1993) concluded that there was some evidence of carcinogenic activity of talc in male F344/N rats based on an increased incidence of benign or malignant pheochromocytomas of the adrenal gland. There was clear evidence of carcinogenic activity of talc in female F344/N rats based on increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and benign or malignant pheochromocytomas of the adrenal gland. There was no evidence of carcinogenic activity of talc in male or female B6C3F1 mice exposed to 6 or 18 mg/m^3 .

Non-asbestiform talc has recently been reviewed by IARC (IARC 2008); however, the monograph is not yet published except for the sections ‘Summary of data reported’ and ‘Evaluation’. Regarding the NTP studies, the IARC Working Group “*did not consider it probable that the increased incidence of pheochromocytomas was causally related to talc, but based on the experimental data available, neither can talc-related effects be excluded.*”

Syrian golden hamsters (50 animals of each sex per group) were exposed to an aerosol of talc baby powder (95% platy talc with trace quantities of magnesite, dolomite, chlorite and rutile) for 3, 30 or 150 minutes per day on five days a week for 30 days (Wehner et al. 1977, 1979 – quoted from IARC 1987a). The mean aerosol concentration was 37.1 mg/m^3 , with a mean respirable fraction of 9.8 mg/m^3 (mass median aerodynamic diameter of 4.9 μm). Two further groups were exposed to talc aerosol for 30 or 150 minutes per day for 300 days or until death. The mean aerosol concentration was 27.4 mg/m^3 , with a mean respirable fraction of 8.1 mg/m^3 (mass median aerodynamic diameter of 6 μm). No primary neoplasm was found in the respiratory system of any hamster. The incidence of alveolar-cell hyperplasia was 25% in the groups exposed to aerosol for 30 or 150 minutes per day for 300 days, compared with 10% in the control group (sham exposed). Non-neoplastic findings are described in section 4.4.1. The IARC Working Group noted the inadequate duration of the study.

Syrian golden hamsters (24 animals of each sex) received 18 weekly intratracheal injections of 3 mg talc (United States Pharmacopeia grade, 93.3% below 25 μm) in saline. The animals were allowed to live out their lifespan (average 50% survival, 46-55 weeks). No respiratory-tract tumour was observed. (Stenbäck & Rowland 1978 – quoted from IARC 1987a). The IARC Working Group noted that the survival was relatively short.

5.7.2 Oral intake

In rats (25 animals of each sex) administered about 50 mg/kg bw/day of commercial talc (characteristics unspecified) in the diet for life (average survival, 649 days), no significant difference in tumour incidence was found in comparison with controls administered standard diet for life (Gibel et al. 1976 – quoted from IARC 1987a).

5.7.3 Dermal contact

No data have been located.

5.7.4 Other routes

IARC (1987a) has summarised a number of other studies in which talc of different grades was administered by various routes of administration, including single intrathoracic or intrapleural injection, subcutaneous injection, and intraperitoneal injection. Tumour incidence was not increased following either the administration of single doses of various talcs to rats by intrapleural administration of talc by four intraperitoneal injections. A single subcutaneous injection of talc in mice did not produce local tumours. The majority of these studies were considered by the IARC Working Group as inadequate.

6 Regulations

6.1 Ambient air

Denmark (C-value): 0.001 mg/m³ (tentative), Main Group 2 (MST 2002).

6.2 Drinking water

6.3 Soil-

6.4 Occupational Exposure Limits

Denmark: 0.3 fibre/cm³, notation for carcinogenic effect (At 2007) Talcum with fibres (CAS-no. 14807-96-6). It should be noted that this CAS-no. is the one for 'non-asbestiform talc'.

ACGIH: 2 mg/m³, respirable fraction. This TLV-TWA applies only to talc dusts containing no asbestos fibres and < 1 % crystalline silica. This value is intended to protect against pulmonary effects. Talc is assigned an A4, Not Classifiable as a Human Carcinogen, notation. (ACGIH 2001 – quoted from Toxline).

Germany: Carcinogenic group 3B (not classifiable). CAS No. 14807-96-6, no asbestos, respirable fraction. (MAK 2006).

6.5 Classification

6.6 IARC

Group 3 (talc not containing asbestiform fibres). Evidence for carcinogenicity to humans and to animals inadequate for talc not containing asbestiform fibres. (IARC 1987a).

Non-asbestiform talc has recently been reviewed by IARC (IARC 2008); however, the monograph is not yet published except for the sections 'Summary of data reported' and 'Evaluation'. Below is the conclusion:

Group 3: Inhaled talc not containing asbestos or asbestiform fibres is not classifiable as to its carcinogenicity to humans. (IARC 2008).

6.7 US-EPA

7 Summary and evaluation

7.1 Description

Cosmetic grade talcum is a fine powder, white to grayish in colour with a greasy feel and lustre. It is insoluble in water.

7.2 Environment

Talc is a naturally occurring mineral. In its pure form, talcum is composed of 63.5% silicium dioxide, 31.7% magnesium oxide, and 4.8% water. Talc ore may contain several other minerals including e.g., calcite, dolomite, magnesite, tremolite, anthophyllite, quartz and serpentines (e.g., chrysotile, the most commonly encountered form of asbestos). Small amounts of aluminium and titanium may substitute to some extent for silicon, and it is common to find iron, nickel, manganese, or chromium substituting to some extent for magnesium.

7.3 Human exposure

The general population is potentially exposed to cosmetic grade talcum (non-asbestiform) through its many uses in consumer products, including pharmaceuticals. Based on these uses, human exposure to talcum can occur via inhalation, ingestion, or dermal exposure.

7.4 Toxicokinetics

Talc particles have been found at autopsy in the lungs of individuals exposed talc.

Following a single, 2-hour, nose-only inhalation exposure to hamsters, 6-8% of the inhaled quantity of talc was deposited in the alveoli; the biological half-life was estimated at 7-10 days. No translocation of talc to liver, kidneys, ovaries or other parts of the body was found.

In rats and mice exposed by inhalation to talc (rats: 2.3-17 mg/m³; mice: 2.2-20.6 mg/m³, 6 hours/day, 5 days/week, for 4 weeks), the resulting lung burdens of talc were 0.08-0.87 mg/g for rats and 0.1-1.2 mg/g for mice.

In rats exposed to talc aerosols (mean respirable dust, 10.8 mg/m³) for three, six and 12 months, talc levels retained in the lung were roughly proportional to the cumulative exposures.

In life-time studies, rats and mice were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation. Lung talc burdens increased progressively from 6 to 24 months in both species and sexes at 6 mg/m³ and in females of both species at 18 mg/m³. In male rats and mice exposed to 18 mg/m³, lung burden remained about the same after 18 months. Lung burdens were generally proportional to exposure concentration.

In studies with rats, mice and guinea-pigs, no intestinal absorption or translocation of ingested talc to the liver and kidneys was detected.

7.5 Human toxicity

7.5.1 Single dose toxicity

Respiratory distress syndrome, which can be fatal, has been described in children following massive accidental inhalation of talcum powder.

7.5.2 Irritation and sensitisation

No data have been located.

7.5.3 Repeated dose toxicity

In cohort mortality studies of workers employed in talc mines and mills, excess in mortality has been observed for non-malignant respiratory disease. One study reported that most of those dying with non-malignant respiratory disease had radiographic evidence of pneumoconiosis (rounded opacities). In an Italian study, significant increases in specific cause of death among miners were found for silicosis and for silico-tuberculosis; however, a high occurrence of silicosis and silico-tuberculosis were also found in the comparison group.

A Norwegian study (Wergeland et al. 1990) did not find an association between respiratory disease mortality and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied.

A cohort mortality and nested case-control study of French and Austrian talc workers (Wild et al. 2002) found a non-significant excess mortality for all non-malignant respiratory diseases in the French cohort due to a significant excess for pneumoconiosis (SMR 5.56, three observed, 95% CI 1.12-16.2). The case-control study of non-malignant respiratory disease showed an increased mortality in the highest exposure groups (odds ratio (OR) 2.5 for a cumulative exposure >800 y.mg/m³) with a significant trend (OR/100 y.mg/m³ 1.08) with cumulative exposure to talc. The authors concluded that the mortality from non-malignant respiratory disease was found to be related to high cumulative exposure to talc dust.

A longitudinal survey of French and Austrian talc workers (Wild et al. 2008) found that the forced expiratory volume in one second (FEV₁) (standardised values based on expected values according to age, sex and height) decreased with total cumulative exposure (FEV₁ decreased by 6.58 ml per 10 years.mg/m³ of the overall cumulative exposure, 95% CI -13.81 to -0.65), but not with the cumulative exposure since inclusion. Similarly, the prevalence of small radiological opacities was found to increase with the exposure estimation at inclusion, but not with the cumulative exposure since inclusion. The mean estimated talc dust concentration during the mean duration of follow-up (14.5 years) was 1.46 mg/m³.

7.5.4 Toxicity to reproduction

No data have been located.

7.5.5 Mutagenic and genotoxic effects

No data have been located.

7.5.6 Carcinogenic effects

In cohort mortality studies, cancer risk was assessed among miners and millers of talc that was reported to contain no more than trace amounts of asbestos. One study showed an excess of lung cancer among underground miners but not among millers. Three other studies suffered, according to IARC (1987a), from methodological limitations and could not be interpreted.

A Norwegian study (Wergeland et al. 1990) did not find an association between lung cancer morbidity and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied.

In a cohort mortality and nested case-control study of French and Austrian talc workers (Wild et al. 2002), mortality from lung cancer was in small excess in both cohorts (France, SMR 1.23, 21 cases observed, 95% CI 0.76-1.89; Austria, SMR 1.06, seven cases observed, 95% CI 0.43-2.19). No increasing trend with cumulative exposure to talc could be found in the case control study of lung cancer. The authors concluded that the small excess in lung cancer does not seem to be attributable to talc.

7.6 Animal toxicity

7.6.1 Single dose toxicity

No data have been located.

7.6.2 Irritation, sensitisation

No data have been located.

7.6.3 Repeated dose toxicity

Studies in rats have revealed local effects in the lungs (fibrosis, chronic inflammatory changes), following inhalation exposure to talc at levels ranging from about 11-380 mg/m³ for 3-9 months. No effects were observed in hamsters exposed by inhalation to talc at 8 mg/m³ for 300 days.

In life-time studies, rats and mice were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation.

In rats, absolute and relative lung weights were significantly greater than those of controls from 6 months of exposure (male rats), and 11 months of exposure (female rats) at 18 mg/m³, and in female rats at the end of the study at 6 mg/m³. At the microscopic examination, a spectrum of inflammatory, reparative, and proliferative processes in the lungs was noted at both exposure levels. The pulmonary lesions were generally similar at the interim evaluations and the end of the study, but varied in incidence, extent and severity with exposure concentration and duration. In exposed rats, there was a concentration-related impairment of respiratory function (reductions in total lung capacity, vital capacity, and forced vital capacity; lung compliance, gas exchange efficiency, and non-uniform intrapulmonary gas distribution), which increased in severity with increasing exposure duration.

In mice, absolute and relative lung weights were significantly greater than those of controls at 12 months and at the end of exposure at 18 mg/m³, and in females at 18 months at 18 mg/m³. The microscopic examination revealed that inhalation exposure was associated with chronic active inflammation and the accumulation of macrophages in the lung at both exposure levels. The pulmonary lesions were generally similar at the interim evaluations and the end of the study, but varied in incidence, extent and severity with exposure concentration and duration. In contrast to rats, hyperplasia of the alveolar epithelium, squamous metaplasia, or interstitial fibrosis was not associated with the inflammatory response in mice.

7.6.4 Toxicity to reproduction

No teratogenic effects were observed in rats, mice, rabbits or hamsters after oral administration of talc.

No inhalation data have been located.

7.6.5 Mutagenic and genotoxic effects

Talc did not induce mutations in *Salmonella typhimurium* strains TA1530 or HisG46, or in *Saccharomyces cerevisiae*, and did not induce chromosomal aberrations in human fibroblasts treated *in vitro*, or chromosomal aberrations in bone marrow cells or dominant lethal mutations in germinal cell in rats following oral administration of talc.

7.6.6 Carcinogenic effects

In rats exposed by inhalation to talc at a mean respirable dust concentration of 10.8 mg/m³ for up to 12 months, one lung adenoma was observed.

In hamsters exposed to an aerosol of talc baby powder, no primary neoplasm was found in the respiratory system of any hamster.

In life-time studies, rats and mice were exposed to aerosols of 0, 6, or 18 mg/m³ talc (non-asbestiform, cosmetic grade, finely powdered) by inhalation. In female rats, the incidences of alveolar/bronchiolar adenoma, carcinoma, and adenoma or carcinoma (combined) were significantly greater at 18 mg/m³ than those of controls. Adrenal medulla pheochromocytomas (benign, malignant, or complex (combined)) occurred with a significant positive trend in male and female rats, and the incidences in the 18 mg/m³ groups were significantly greater than those of controls. In mice, the incidences of pulmonary neoplasms in exposed and control groups of mice were similar.

In rats administered about 50 mg/kg bw/day of commercial talc in the diet for life, no significant difference in tumour incidence was found in comparison with controls administered standard diet for life.

7.7 Evaluation

The term 'talc' refers to both mineral talc and industrial products that contain mineral talc and are marketed under the name talc. Mineral talc is usually platy (non-fibrous) but may also occur as asbestiform fibres. Commercial talc is categorised into cosmetic grade, which is free of asbestos, and industrial grade, which contains other minerals including asbestos. In this evaluation, only the non-fibrous cosmetic grade talc, i.e., non-asbestiform talc in powder form is considered in relation to an estimation of a health-based quality criterion in air. It should be noted that asbestiform talc must not be confused with talc that contains asbestos.

The available toxicokinetic studies indicate that talc, including the respirable fraction, is not absorbed following inhalation, but retained in the lung tissue. Lung burdens are generally proportional to the exposure concentration indicating that the clearance of talc from the lung is impaired to a greater extent with increasing exposure concentrations.

The information regarding acute toxicity of talc is limited to case stories reporting respiratory distress syndrome, which can be fatal, in children following massive accidental inhalation of talc powder. No data have been located regarding irritation or sensitisation.

In humans and experimental animals, the effects of repeated exposure to talc are dependent on the route of exposure, the dose and the properties of the talc.

In epidemiological studies (cohort mortality studies) of workers employed in talc mines and mills, as summarised by IARC (1987a), excess in mortality has been observed for non-malignant respiratory disease. One study reported that most of those dying with non-malignant respiratory disease had radiographic evidence of pneumoconiosis (rounded opacities). A review of epidemiological studies published in 1992 concluded that the pulmonary damage induced by exposure to talc varies depending on the precise composition of the inhaled dust and the clinical symptoms and the pulmonary pathology associated with talc associated lung diseases were reported to be similar to those of other pneumoconioses. According to IARC (2008), the talc pneumoconiosis is somewhat more prevalent and severe among workers exposed to talc containing asbestiform (fibrous) minerals and/or asbestos than among those exposed to talc without such contaminants. The role of quartz and asbestos in the observed pneumoconiosis could not be ruled out. Therefore, these epidemiological studies are considered as being inadequate in relation to an estimation of a health-based quality criterion in air.

Two mortality studies have been published since 1987 and therefore, not included in the IARC 1987 evaluation (IARC 1987a):

A Norwegian study (Wergeland et al. 1990), did not find an association between respiratory disease mortality and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied. There was one observed death among miners (2.5 expected) and two observed deaths among millers (8.4 expected); the diagnosis was pneumonia in all three cases. No kind of pneumoconiosis was recorded as the main cause of death.

A cohort mortality study of French and Austrian talc workers (Wild et al. 2002) found a non-significant excess mortality for all non-malignant respiratory diseases in the French cohort due to a significant excess for pneumoconiosis (SMR 5.56,

three observed, 95% CI 1.12-16.2). The nested case-control study of non-malignant respiratory disease showed an increased mortality in the highest exposure groups with a significant trend with cumulative exposure to talc. The authors concluded that the mortality from non-malignant respiratory disease was related to the high cumulative exposure to talc dust.

As these two epidemiological studies are mortality studies, there is no information regarding respiratory effects in general. Furthermore, it is not possible to evaluate an exposure-effect relationship based on the exposure assessment in these studies. Therefore, these two studies are considered as being inadequate in relation to an estimation of a health-based quality criterion in air.

A longitudinal survey of French and Austrian talc workers (Wild et al. 2008) found that the prevalence of small radiological opacities and decrease in lung function parameters were related to cumulative exposure at inclusion in the study, but not with the cumulative exposure during the study period (i.e., since inclusion). The authors concluded that, although early exposure levels to talc as assessed at inclusion were associated with decreased lung function and an increased prevalence of small radiological opacities, there was no evidence of detrimental effects of talc exposure, as assessed within the study period, on lung function and small radiological opacities. The mean estimated talc dust concentration during the mean duration of follow-up (14.5 years) was 1.46 mg/m^3 .

It is not possible to evaluate an exact exposure-effect relationship based on the exposure assessments in this study. However, as no detrimental effects were observed at the mean estimated talc dust concentration (1.46 mg/m^3) during the study period (mean duration of 14.5 years), this concentration could be interpreted as a No Observed Adverse Effect Concentration (NOAEC) for talc induced lung effects.

A number of repeated dose toxicity studies in rats, summarised by IARC (1987a) and NTP (1993), revealed local effects in the lungs (fibrosis, chronic inflammatory changes), following inhalation exposure to talc at levels ranging from about $11\text{-}380 \text{ mg/m}^3$ for 3-9 months; no effects were observed in hamsters exposed by inhalation to talc at 8 mg/m^3 for 300 days. These studies suffer from several limitations and are therefore, considered as being inadequate in relation to an estimation of a health-based quality criterion in air.

NTP (1993) has carried out inhalation life-time studies in rats and mice exposed to aerosols of 0, 6, or 18 mg/m^3 talc (non-asbestiform, cosmetic grade, finely powdered). The principal toxic lesions in rats included chronic granulomatous inflammation, alveolar epithelial hyperplasia, squamous metaplasia and squamous cysts, and interstitial fibrosis of the lung. These lesions were accompanied by impaired pulmonary function characterised primarily by reduced lung volumes, reduced lung compliance, reduced gas exchange efficiency, and non-uniform intrapulmonary gas distribution. In mice, inhalation exposure to talc produced chronic inflammation of the lung with the accumulation of alveolar macrophages. The pulmonary lesions were noted at both exposure levels, but varied in incidence, extent and severity with exposure concentration and duration. Based on these studies, a LOAEC of 6 mg/m^3 is considered for talc induced lung effects.

The available data on reproductive toxicity is inadequate; however, as talc does not appear to be absorbed following inhalation, the risk for reproductive toxicity is considered as being very low following inhalation exposure to talc.

The available data on genotoxicity, although limited, indicate that talc does not have a genotoxic potential.

In several mortality studies, summarised by IARC (1987a), cancer risk was assessed among miners and millers of talc that was reported to contain no more than trace amounts of asbestos. A cohort mortality study showed an excess of lung cancer among underground miners but not among millers; however, according to IARC, a contributory etiological role of radon daughters to the lung cancer risk in miners could not be excluded. Three other studies published suffered, according to IARC, from methodological limitations and could not be interpreted. Based on these studies, IARC (1987a) has concluded that there is inadequate evidence for the carcinogenicity to humans of talc not containing asbestiform fibres.

In contrast, IARC (1987a) has concluded that there is sufficient evidence for the carcinogenicity to humans of talc containing asbestiform fibres based on studies of miners and millers exposed to talc containing asbestiform tremolite and anthophyllite that showed an excess of lung cancer and one case of mesothelioma.

Since the IARC 1987 evaluation (IARC 1987a), a number of studies have been published. One of these is a Norwegian study (Wergeland et al. 1990), which did not find an association between lung cancer morbidity and exposure to non-asbestiform talc with low quartz content in the one mine and one mill studied. Another one is a cohort mortality and nested case-control study of French and Austrian talc workers (Wild et al. 2002), in which mortality from lung cancer was in small excess in both cohorts, but no increasing trend with cumulative exposure to talc could be found in the case control study of lung cancer. The authors concluded that the small excess in lung cancer does not seem to be attributable to talc.

Non-asbestiform talc has recently been reviewed by IARC (IARC 2008); however, the monograph is not yet published except for the sections 'Summary of data reported' and 'Evaluation'. It is obvious from the summary that new epidemiological evidence has been available for the IARC Working Group, including the two above-mentioned studies. The Group concluded that there is inadequate evidence in humans for the carcinogenicity of inhaled talc not containing asbestos or asbestiform fibres.

IARC (1987a) has summarised a number of carcinogenicity studies in different animal species (rats, mice, hamsters) administered talc of different grades by various routes of administration. The majority of these studies were considered by the IARC Working Group as inadequate and overall, the Group concluded that there is inadequate evidence for carcinogenicity of talc to experimental animals.

Under the conditions of the life-time inhalation studies in rats and mice, the NTP (1993) concluded that there was some evidence of carcinogenic activity of talc in male rats based on an increased incidence of benign or malignant pheochromocytomas of the adrenal gland. There was clear evidence of carcinogenic activity of talc in female rats based on increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and benign or malignant pheochromocytomas of the adrenal gland. There was no evidence of carcinogenic activity of talc in male or female mice.

Goodman (1995) voted against these conclusions when the Talc Report was reviewed by the NTP Board of Scientific Counselors for the following reasons: "*A thorough evaluation of lung toxicity revealed that talc-induced lung tumours occurred only in the group of animals that exhibited the most profound degree of*

chronic toxicity. However, these data were presented as empirical observations rather than discussed in a manner that would relate them to the risk assessment implications of the bioassay, i.e., relevant data were collected but not "used." In addition, the evaluation of the pheochromocytomas was inadequate because it failed to place sufficient emphasis on the spontaneous incidence of this tumour in rats. The appropriate conclusions are, according to Goodman, 1) the data do not indicate that the pheochromocytomas were treatment-related; 2) the maximum tolerated dose (MTD) was exceeded in the female rats exposed to the high dose; and 3) talc is not expected to cause lung tumours under conditions of exposure that fail to result in marked chronic lung toxicity."

Non-asbestiform talc has recently been reviewed by IARC (IARC 2008); however, the monograph is not yet published except for the sections 'Summary of data reported' and 'Evaluation'. Regarding the NTP studies, the IARC Working Group did not consider it probable that the increased incidence of pheochromocytomas was causally related to talc, but based on the experimental data available, neither can talc-related effects be excluded. Based on the available evidence, the Group concluded that there is limited evidence in experimental animals for the carcinogenicity of talc not containing asbestos or asbestiform fibres.

Wehner (2002) has criticised the conclusion 'Talc is carcinogenic': "*Concerns that cosmetic talc might be carcinogenic are addressed and shown to lack persuasive scientific support. These concerns are based 1) on several, but not all, retrospective epidemiological, statistically barely significant case-control studies of questionable biological import (Their results lack dose-response relationships, are inconsistent and ambiguous, and are therefore inconclusive); 2) on one inhalation study in animals whose results, according to a panel of experts, "cannot be considered as relevant predictors of human risk," a position shared by other experts in the field; and 3) on elevated incidence of lung cancer in pottery workers. These workers were occupationally exposed several decades ago to nowadays impermissible concentrations of aerosols comprising a multitude of industrial dusts. To construe a risk for the consumer of pure cosmetic or pharmaceutical-grade talc under consumer conditions, based on these findings, lacks scientific support. Talc is not genotoxic, is not carcinogenic when injected into ovaries of rats, does not cause cancer decades after pleurodesis, and induces apoptosis in vitro in human mesothelioma cells but not in normal mesothelial cells. There is no credible evidence of a cancer risk from inhalation of cosmetic talc by humans. Considering talc a carcinogen lacks convincing scientific documentation.*"

IARC (2008) concluded that inhaled talc not containing asbestos or asbestiform fibres is not classifiable as to its carcinogenicity to humans (Group 3).

Overall, there is some evidence that talc has the potential to induce pulmonary neoplasms in female rats. These tumours, which were only observed at the highest concentration, are considered to be a result of the deposition of talc dust particles in the lung tissues, i.e., an overload phenomenon. In the NTP (1993) studies, lung burdens were generally proportional to the exposure concentration indicating that the clearance of talc from the lung is impaired to a greater extent with increasing exposure concentrations. Non-neoplastic pulmonary lesions were noted at both exposure levels in both rats and mice, but varied in incidence, extent and severity with exposure concentration and duration.

Pheochromocytomas of the adrenal medulla (benign and malignant combined) were observed in rats of both sexes. According to Ozaki et al. (2002), hypoxemia resulting from lung alterations in exposed rats has been hypothesised to stimulate catecholamine secretion from the adrenal medulla where chronic hyperactivity

leads to pheochromocytomas. Thus, pheochromocytomas in the NTP (1993) study could be secondary to chronic lung injury and hypoxia. Based on these studies, a LOAEC of 6 mg/m³ is considered for talc induced lung effects.

7.7.1 Critical effect and NOAEL

The critical effect following inhalation exposure to talcum, i.e., the finely powdered non-fibrous cosmetic grade talc, in relation to an estimation of a health-based quality criterion in air is considered to be the non-neoplastic pulmonary lesions noted in both humans and in experimental animals.

In general, the epidemiological studies suffer from a number of limitations and are considered as being inadequate in relation to an estimation of a health-based quality criterion in air. One exception is the very recent longitudinal survey of French and Austrian talc workers (Wild et al. 2008). It is not possible to evaluate an exact exposure-effect relationship based on the exposure assessment in this study. However, as no detrimental effects (as assessed by standard lung function tests and standard chest x-rays for radiological opacities) were observed at the mean estimated talc dust concentration (1.46 mg/m³) during the study period (mean duration of 14.5 years), this concentration could be interpreted as a No Observed Adverse Effect Concentration (NOAEC) for talcum induced lung effects. It should be noted, however, that the detrimental lung effects in question are only observed following cumulative exposure to relatively high concentrations (i.e., above the concentrations measured in the Wild et al. (2008) study) for many years. Therefore, the follow-up period of about 15 years might not be long enough in order to reveal the detrimental lung effects. It is also noteworthy that the workers have been exposed to talc containing a minor amount of quartz (below 1% for the French talc workers but up to 3% for the Austrian talc workers).

Based on the NTP (1993) life-time studies with rats and mice, a LOAEC of 6 mg/m³ is considered for talcum induced lung effects. It is noteworthy that the talc used for these studies was of cosmetic grade, non-asbestiform (i.e., non-fibrous version), finely powdered and respirable (mass median aerodynamic diameter of 2.7 µm), i.e., talcum as defined in this evaluation (see the introduction to this section).

As both the human data and the data from the NTP (1993) study are considered as being adequate in relation to an estimation of a health-based quality criterion in air, both scenarios are included (see Chapter 7).

8 Quality criterion in ambient air

The health-based quality criterion in air QC_{air} is estimated based on 1) human data and 2) animal data.

Scenario one - human data:

The quality criterion in air QC_{air} is calculated based on a NOAEC of 1.5 mg/m^3 (rounded figure from the mean estimated talc dust concentration of 1.46 mg/m^3) for talc induced lung effects in the longitudinal survey of French and Austrian talc workers (Wild et al. 2008). As the mean exposure is assumed to be discontinuous (8 hours/day, 5 days/week), the NOAEC of 1.5 mg/m^3 is recalculated to a NOAEC of 0.36 mg/m^3 for continuous exposure [$1.5 \times 8/24 \times 5/7$]:

$$\begin{aligned} QC_{\text{air}} &= \frac{\text{NOAEC}}{UF_I * UF_{II} * UF_{III}} = \frac{0.36 \text{ mg/m}^3}{1 * 10 * 10} \\ &= 0.0036 \text{ mg/m}^3 \end{aligned}$$

The UF_I accounting for interspecies variability is set to 1 as human data are used. The UF_{II} accounting for intraspecies variability is set to 10 reflecting the range in biological sensitivity within the human population. The UF_{III} is set to 10 because the data on which the NOAEC is based are not sufficient in order to characterise an exact exposure-effect relationship and because the follow-up period of about 15 years might not be long enough in order to reveal the detrimental lung effects.

Scenario two – animal data:

The quality criterion in air QC_{air} is calculated based on a LOAEC of 6 mg/m^3 for talc induced lung effects in the NTP (1993) life-time studies with rats and mice. As the exposures were discontinuous (6 hours/day, 5 days/week), the LOAEC of 6 mg/m^3 is recalculated to a LOAEC of 1.1 mg/m^3 for continuous exposure [$6 \times 6/24 \times 5/7$]:

$$\begin{aligned} QC_{\text{air}} &= \frac{\text{LOAEC}}{UF_I * UF_{II} * UF_{III}} = \frac{1.1 \text{ mg/m}^3}{2.5 * 10 * 10} \\ &= 0.0044 \text{ mg/m}^3 \end{aligned}$$

The UF_I accounting for interspecies variability is set to 2.5^1 assuming that humans are more sensitive than animals. The UF_{II} accounting for intraspecies variability is set to 10 reflecting the range in biological sensitivity within the human population.

¹ According to the REACH Technical Guidance Document, the default interspecies factor is 2.5 for local effects in the lungs.

The UF_{III} is set to 10 because of using a LOAEC in stead of a NOAEC and as no data on the steepness of the dose-response curve is available.

A QC_{air} of 0.004 mg/m^3 has been calculated based on both the human data and the animal data (rounded value from 0.0036 and 0.0044 mg/m^3 , respectively). The C-value at present for talcum is 0.001 mg/m^3 and talcum is placed in Main Group 2 (MST 2002). A C-value of 0.004 mg/m^3 and placing in Main Group 2 is proposed.

8.1 C-value

0.004 mg/m^3 , Main Group 2.

It should be noted that this C-value is only valid for cosmetic grade talcum (CAS No. 14807-96-6), finely powdered and containing no asbestos, quartz or fibres, or other carcinogenic compounds.

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Talcum, cosmetic grade (non-fibrous)

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to talcum, cosmetic grade, non-fibrous. This resulted in 2010 in the present report which includes a health-based quality criterion for the substance in ambient air.



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