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Health-based recommended occupational exposure limit for talc dusts

Dutch expert committee for occupational standards
(Met Nederlandse samenvatting)

This is a report of the Dutch Expert Committee for occupational standards (DEC). The draft-document has been prepared by A.A.E. Wibowo

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NEDERLANDSE SAMENVATTING
TALKSTOF

1. FYSISCHE EN CHEMISCHE EIGENSCHAPPEN

Talkstof is een gehydrateerd magnesiumsilikaat(poeder) met een basisformule: $(Mg.Fe^{+2})_3Si_4O_{10}(H_2O)$. Het heeft de vorm van dunne tabulairvormige kristallen met een breedte tot 1 cm. CAS reg. nr. 14807-96-6.

2. MONITORING

Het komt vaak voor dat talkstof gecontamineerd wordt met andere mineralen waarvan sommige biologisch aktief zijn. Daarom is men aangewezen op een analyseprotocol om onderscheid te kunnen maken tussen de contaminanten. De volgende methoden kunnen gebruikt worden:

- Fase-contrast optische mikroskopie
- Rö-stralen diffractie-analyse
- Analytische electronenmikroskopie en geselecteerde-area diffractie.

Biologische monitoring is niet toepasbaar bij blootstelling aan talkstof.

3. GRENSWAARDEN

De grenswaarden (MAC) in Nederland voor talkstof (vrij van asbestvezels en respirabel quartz <5%) zijn 3,0 mg/m^3 als respirabel stof en 6,0 mg/m^3 als totaal stof, tgg-8 uur. In de VS alsook in Duitsland is de grenswaarde voor talkstof (vrij van asbestvezels) 2,0 mg/m^3 als respirabele deeltjes, tgg-8 uur. Zweden en de Sovjet Unie hebben geen grenswaarde voor talkstof.

4. TOXICOKINETIEK

Samenvattingen van de humane en dierexperimentele gegevens leiden tot de volgende conclusie: de depositie van talkstof in de longen na inhalatoire blootstelling is afhankelijk van de aerodynamische diameter van de partikeldeeltjes. De biologische half-waarde tijd van talk in de longblaasjes wordt geschat op enkele dagen tot weken. Talk wordt niet geresorbeerd in de bloedstroom; geen translocatie vindt plaats naar andere delen van het lichaam. De talkbelasting van de longen is afhankelijk van de mate en duur van de blootstelling. Talk in de longen verspreid zich bij voorkeur naar het interstitiële weefsel, daarna naar perivasculaire en peribronchiale weefsels en het minst naar subpleurale weefsels. Bij de mens vindt men een lineair verband tussen de gemiddelde siliconengehaltes in de longen die gemeten worden met Röstraling en de duur van blootstelling aan respirabel talkstof.

5. EFFECTEN

Dierexperimentele gegevens tonen aan dat zuiver talkstof een fibrogenische stof is; inhalatoire blootstelling veroorzaakt longfibrose. Geen maligne longtumoren komen voor bij ratten en hamsters blootgesteld gedurende langere tijd aan kosmetische graad talkstof via inhalatie. Ook intratracheale toediening van kosmetisch graad talkstof gedurende 120 weken bij hamsters veroorzaakt geen tumoren. Talkstof is niet mutageen en het veroorzaakt geen afwijkingen van de chromosomen. Talkstof is niet teratogeen via orale toedieningsroute.

Bij mensen die aan talkstof blootgesteld worden tijdens het werk zijn de longen het doelorgaan. De meest voorkomende aandoening is talkpneumoconiose. Waarschijnlijk speelt accumulatie van talk in de longen een belangrijke rol bij de pathogenese. Gevallen van mesotheliomen van het borstvlies worden gemeld bij werknemers blootgesteld aan industriegraad talkstof, wat waarschijnlijk is gecontamineerd met asbestvezels.
Een van de eerste tekenen van afwijkingen aan de longen is vermindering van de longfunctie, o.a. verlaging van de FEV_1, FEV_1/FVC ratio en MMEF.

6. EVALUATIE EN ADVIES

In de gezondheidskundige evaluatie van blootstelling aan talkstof dient men onderscheid te maken tussen twee verschillende soorten van talk:

(1) *Kosmetische graad talkstof* is talk die gedolven wordt uit geselecteerde mijnen met de begrenzing dat minstens 90% van het stof vrij moet zijn van asbestvezels, maar andere mineralen kunnen voorkomen in minimale hoeveelheden.

(2) *Industrie graad talkstof* is talk bestaande uit een mengsel van talk met andere soorten mineralen om het stof van de gewenste fysische eigenschappen te voorzien.

De voorgestelde advieswaarde is gebaseerd op gegevens uit de epidemiologische studies waarbij afwijkingen van de longfunctie gebruikt worden als graadmeter. Men schat dat de minimale nadelige effectconcentratie voor respirabel *kosmetisch graad talkstof* bij gehaltes van 0,50-1,8 mg/m^3 liggen. Er zijn geen aanwijzingen naar het voorkomen van kanker bij blootstelling aan *kosmetisch graad talkstof*, dit is wel het geval bij blootstelling aan *industrie graad talkstof* dat waarschijnlijk gecontamineerd is met asbestvezels.

Het advies luidt dan als volgt:
Voor *kosmetisch graad talkstof* geldt een advieswaarde van 0,25 mg/m^3 respirabele fraktie, tgg-8 uur.

Voor *industrie graad talkstof* is het afhankelijk van de gehaltes van quartz en asbestvezels zoals bepaald met de PCOM.
Indien vrij van quartz en asbestvezels: 0,25 mg/m^3 respirabele fraktie, tgg-8 uur. Indien gecontamineerd met quartz en/of asbestvezels dan gelden de advieswaarden die voor deze stoffen zijn voorgeschreven.

(Datum afronding advies: juni 1991)

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1 IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, MONITORING

1.1 IDENTITY

1.1.1 Structure

Talc is a hydrous magnesium silicate whose basic formula is $(Mg.Fe^{+2})_3Si_4O_{10}(OH_2)$ with theoretical weight percentages as follows: 63% SiO_2, 32% MgO and 5% H_2O.Fe^{+2} may substitute for as much as 10% of the magnesium atoms. Aluminium in trace amounts may also substitute for magnesium and silicon. The term "talc" applies to a group of minerals with compositions ranging from those which closely approach the theoretical composition above to others which, while containing appreciable amounts of magnesia, are essentially mixtures of silicates. Serpentine chlorites, silicates, tremolite, anthophyllite, diopside, soapstone, pyrophyllite and steatite have been categorised as talcs or talcose rocks. The latter terms refer to talcose rocks containing no more than 1.5% lime. 15% iron oxides and 4% aluminium oxide.

1.1.2 Chemical names and synonyms/Registry numbers

Chem. Abstr. name	: Talc
CAS Registry number	: 14807 - 96 - 6
Synonyms	: Soapstone
	Steatite
	Talcum
Trade names	: Agalite
	Asbestine etc.

1.2 PHYSICAL AND CHEMICAL PROPERTIES

(IARC), 1987; Boundy et al., 1979)

Molecular formula	: $(Mg.Fe^{+2})_3Si_4O_{10}(OH_2)$
Refractive indices	: 1.54 - 1.6
Hardness	: 1 on Mohs' scale

Specific gravity	: 2.58 - 2.83
Cleavage	: (001) perfect
Colour	: pale-green to dark-green or greenish-grey; also white, silvery-white, grey, brownish, translucent, pearly, greasy or dull.
Description	: commonly thin tabular crystals, up to 1 cm in width. Usually massive, fine grained, compact; also as foliated or fibrous masses or in globular stellate groups.

The chemistry of talc shows little variation, indicating that only limited substitution of ions takes place in the mineral lattice. When expressed in the standard oxide form, the ideal chemical composition is: 31.7% MgO
63.5% SiO_2
4.8% H_2O

Small amounts of aluminium and titanium may substitute to some extent for silicon; it is more common to find iron, nickel, manganese or chromium substituting to some extent for magnesium.

1.3 ANALYTICAL METHODS

1.3.1 Environmental monitoring

The strategy of environmental monitoring should be directed to identification and followed by measurement of the dust. Because talc is frequently contaminated with other minerals, some known to be biologically active, an analytical protocol is often required that can be distinguished among these contaminants:

- Phase contrast optical microscopy (PCOM): a conventional technique for the identification of minerals. A microscope equipped with bright-field illumination and polarized light optics.

- X-ray diffraction analysis, both continuous- and step-scan modes may be used for quantitative determination of contaminating minerals in talc, including the selection of talc and reference materials, the preparation of standard dilutions of fibers in talc to ensure sensitivity and reproducibility, the selection of characteristic X-ray reflections to be scanned, and instrumental technique. Tremolite, chrysotile and anthophyllite impurities in talc can be determined at levels as low as 0.1-2%.

- Analytical electron microscopy and selected-area diffraction are methods for the determination of the morphological, structural and chemical information on single particles of talc and associated minerals.

Note: Phase contrast microscopy may suffice in an asbestos environment, but the resolution limitations of optical microscopy and the inability to distinguish rolled talc particles and talc "shards" from actual asbestos fibers will allow only a crude determination of the total fiber exposure (Boundy et al., 1979).

For measurement of the dust the same method can be used as performed for inert dust (the gravimetric method).

1.3.2 Biological monitoring

Conventional biological monitoring techniques are not applicable for exposure to talc.

A method for Biological Effect Monitoring has been reported by Kung et al. (1984). They found the "pulmonary blue bodies" in the bronchial brushing, aspiration and washing specimens of a patient with evidence of pulmonary talcosis. Pulmonary blue bodies are unusual structures mainly composed of calcium carbonate and most commonly seen in lungs of patients with the desquamative type of interstitial pneumonitis. The following method for analysis is used: the bronchial brush smears, aspiration, and washing specimens are fixed in 95% ethanol and stained with hemotoxylin and eosin. Of the three bronchial smears prepared, one is used for examination for calcium carbonate. The cover slip is removed and the slide coated with carbon and subjected to scanning electron microscopy and X-ray analysis. The blue bodies are isolated and small clusters of ovoid bodies that vary from 15 to 40 um in their largest dimension. The larger ones have a central laminated refractile core that is brownish, rimmed by a layer of amorphous finely granular blue substance. Under polarized light, the central laminated core is birefringent and varigated in color. The smaller bodies are mostly amorphous and blue and are not birefringent. The structures are extracellular in location.

2 SOURCES OF EXPOSURE

2.1 NATURAL OCCURRENCE

Talc rocks are formed by several complex geological processes reacting upon many chemically diverse preexisting rock types. Hydrothermal alterations of magnesia- and silica-rich ultramatic rocks, under a range of low to moderate temperatures and pressures, may produce talc, thermal metamorphosis of silica-rich dolomite will also produce talc (IARC, 1987).

2.2 MAN-MADE SOURCES

2.2.1 Production

The abundance of talc and the facility of mining it, combined with its many desirable functional properties, have made it an important industrial mineral. Mining of talc for commercial purposes probably started several hundred years ago when talc blocks were used for building materials and cooking utensils. The world reserve base of talc and the related aluminium silicate, pyrophylite, is estimated to be 1200 million tonnes. The latest technology in talc refining employs flotation separation, drying of the filtered powder cake and sizing or further grinding before shipping. Talc is mined in over 40 countries and is used in numerous manufacturing industries in over 60 countries.

2.2.2 Uses

The valuable qualities of talc in industry are its extreme softness, whiteness (when pure), good hiding power, high surface area, high slip or lubricating power, chemical inertness, low electrical and heat conductivity, oil absorption properties and high refractoriness. Because of this great versatility talc in a variety of grades is put to a large number of industrial uses, but only the most common are referred to:

- paints; talc is used as a filler and inert extender. Fibrous talc (asbestine) is also widely employed because its good suspending powers reduce settling in the can and also increase the mechanical strength of paint films

- cosmetic and pharmaceutical industry; high grade talcs are used for e.g. face powders, talcum powders, polishing tablets etc. The particle size of good cosmetic grade talc lies between 0.3 to 50 um. Quartz and other harsh minerals should be absent or only trace amounts present. The only impurity should be calcium sulphate
- ceramics; talc is employed for a variety of purposes
- roof felting industry; where the lubricating properties of talc are used to prevent the layers sticking when rolled and to increase resistance to fire and weather
- rubber industry; where the lubricating properties are exploited as a dusting agent to prevent adhesion of the rubber in the moulds and to provide smooth extrusion It is also used as a filler in hard rubber goods
- fertilizer industry; where talc is used as an anticaking agent in the manufacture of fertilizers
- refractory materials; where talc is used as a refractory filler for moulds and cores in both ferrous and non-ferrous castings
- paper industry; because of its whiteness, good retention and ability to improve the gloss, opacity and brightness of paper, talc may be substituted for china clay as a coating and filler of paper
- textile industry; where finely ground talc is used for "loading" and bleaching cotton sacs, cordage, string and rope.

3 ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 ENVIRONMENTAL LEVELS

3.1.1 Water and food

No data are available on levels of talc in drinking water and food.

3.1.2 Air (occupational)

Exposure to talc dust occurs during mining, crushing, separating, bagging, loading and in end-use facilities, such as rubber dusting and addition of talcs to ceramic clays and glazes. Since industrial talc is a mixture of various associated minerals, occupational exposure is to a mixture of mineral dusts. Nearly all measurements made prior to approximately 1970 were done by collecting particles in an impinger and counting them by optical microscopy. Concentrations were then expressed as millions of particles per cubic foot of air (mppcf).

Only limited information is available about exposures in secondary industries in which talc is used or further processed (IARC, 1987). Personal air samples collected in a rubber band production plant, where housekeeping, ventilation and work practices were poor and in which talc was used as an antistick agent, had time-weighted average respirable dust concentrations of 2.5-7.8 mg/m^3 (average 4.8 mg/m^3) for extruders, 5.3 and 6.1 mg/m^3 for vulcanizers, and 0.9 and 1.3 mg/m^3 for cutters. Total dust exposures were found to range from 5.4-199 mg/m^3. The talc was reported to contain 2-3% free silica. Fibre exposures as measured by phase-contrast optical microscopy, ranged from 4.7-19.2 fibres >5 um/cm^3.

Fine et al. (1976) performed environmental monitoring in two rubber plants using personal samplers with constant flow rates. In one plant they found a range of the average Mass Respirable Dust Concentrations of 0.51 mg/m^3 (Hose Extruding Dept.)-3.55 mg/m^3 (Rubber Band Area). In the other plant they found a range of 0.47 mg/m^3 (Tuber Operator)-1.41 mg/m^3 (Truck and Bus Inner Tubes). The talc was characterized by a low content of silica and fiber. Eighteen of twentyone samples analyzed for free silica contained less than 1%. The twelve samples counted for fibers by the standard asbestos technique showed less than 2 fibers/ml.

Gamble et al. (1979) reported on collecting personal air samples from miners and millers who worked in the New York State deposits in St. Lawrence County. They were collected on membrane filters and were analyzed gravimetrically for total dust and by rontgenographic diffraction for percent of free silica. Area samples for total particulate and fibers were also collected. The highest level of free silica was 0.04 mg/m^3. Most workers sampled had twa exposures to free silica of less than 0.02 $\mu g/m^3$. The mean twa exposures to respirable particulate in the mine ranged from 0.23 to 1.20 mg/m^3, and in the mill from 0.25 to 2.96 mg/m^3. Airborne fibers collected in the mine were identified as 38% anthophyllite, 19% tremolite and 3% chrysotile; 39% were unidentified. In the mill, 45% of the airborne fibers were antophyllite, 12% were tremolite and 2% chrysotile; 38% remained unidentified. A median fiber diameter of 0.19 and 0.13 µm was observed for tremolite and anthophyllite; in the mine, median fiber lengths were 1.6 and 1.5 µm for tremolite and anthophyllite, respectively, and were 0.1 µm shorter for each in the mill.

Wegman et al. (1982) reported talc in air was found to be essentially free from silica and asbestos in three talc companies in Vermont, USA. A total of 312 personal (lapel) respirable mass samples were taken with a mass respirable sampler at a flow rate of 1.7 l/min. Exposure levels were found to be below 3.0 mg/m^3 of respirable dust and the geometric mean exposure was 1.8 mg/m^3 of respirable dust. On the other hand Dement and Zumwalde (1979) studying mine and mills in the Gouverneur Talc District in the Upper New York State, USA, reported that mineral talc constituted 14-48% of the products, with other major components being tremolite (37-59%), anthophyllite (4.5-15%) and the serpentines, lizardite and antigorite (10-15%). The mean respirable dust concentration in the mine was 0.86 mg/m^3 (range 0.23-1.29 mg/m^3) and in the mill 0.86 mg/m^3 (range 0.25-2.95 mg/m^3).

3.2 HUMAN EXPOSURE

3.2.1 General population

There are no data available on exposure of the general population to industrial talc. One may assume that people living nearby mining and milling operations are at risk for exposure.

At the other hand a risk of exposure to cosmetic talc in the general population is more plausible. Talcum powder is one of the most widely used of all bath products. It is mainly comprised of talc, perfume and antibacterial agent. Talc is also a major component of face powders, compact and cake make-up, certain eye-liners, liquid make-up, rouge, foot powders, deodorants, sunscreens, and nail polishing powders. Talc is also used in the manufacture of many other commonly used products including chalks, crayons, shoe polishes, paints, soaps, rubber products, polished rice, molded candy, pills and floor waxes. It is assumed that most of these exposures occur at short-duration.

3.2.2 Occupational population

The greatest human exposure to talc dust is when it is used industrially or while it is mined or milled. For industries with possible exposure to talc dust see Chapter 2.2.2.

4 GUIDELINES AND STANDARDS

4.1 GENERAL POPULATION

There are no standards for talc in ambient air levels.

4.2 OCCUPATIONAL POPULATION

Country (years)	Standards	Comments
The Netherlands (1989)		
Talc (free from asbestos and respirable quartz < 5%)	3.0 mg/m^3, repirable dust	t.w.a.-8 h
	6.0 mg/m^3, total dust	t.w.a.-8 h
	0.7x10^9 particles	With the assumption that 0.2x10^9 particles are equal to 1 mg/m^3 respirable dust and that 50% of total dust consists of respirable dust.
USA - ACGIH (1989)		
Talc (containing no asbestos fibers)	2.0 mg/m^3, respirable dust (1983)	t.w.a.-8 h
Talc (containing asbestos fibers)	Use asbestos TLV's however should not exceed 2 mg/m^3 respirable dust (1985)	
Federal Republic of Germany - DFG (1989)		
Talc (without asbestos fibers)	2.0 mg/m^3, calculated as fine dust	Fine dust is defined as dust which can reach the alveolar area of the lungs.
Sweden - NSBOSF (1987)		
Talc	none	-
USSR (1987)		
Talc	none	-

5 TOXICOKINETICS

5.1 INHALATION KINETICS; HUMAN DATA

There are only a few human data on the kinetics of talc in exposure by inhalation. Talc particles have been found at autopsy in the lungs of cases of talc pneumoconiosis (IARC, 1987). Talc in the form of platy or elongated particles has been found at autopsy in the lungs of urban residents, farmers, asbestos miners and drug addicts. It has been reported to be concentrated in lung scar tissue.

Vallyathan et al. (1981) studied the pulmonary tissue from seven deceased men who had been employed in the mining and milling of talc that contained minimal amounts of crystalline silica and asbestiform minerals in Vermont, USA. The lung samples from the seven cases were processed for light microscopy and ten serial sections of 7 µm diameter were obtained. Examination was done by scanning electron microscopy, back scattered electron imaging, X-ray mapping and X-ray energy spectrometry. Elemental analysis was also performed using a semiquantitative X-ray analysis technique. For a control group eight adult males matched for age by decade with the exposed group were selected. Microscopic evaluation revealed accumulation of birefringent dust particles in perivascular and peribronchial scars. The amounts of particles were greatest in the lungs of those with prolonged exposure histories. X-ray energy spectrometry analysis of lesions containing dust revealed large amounts of both magnesium and silicon in combination with small amounts of aluminium and iron, which were charateristic for all exposed individuals. The analysis of silicon for all seven cases showed a linear correlation with the years of talc exposure. A positive correlation (r^2=0.81) was obtained at a significance of p>0.01 (see Figure 1). Quantitative elemental analysis of three cases and the control group showed the following levels:
The distribution of the major elements (Mg, Al, Si and Fe) in anatomic sites in the left lung of one case is shown in Figure 2. A significant difference in the lobar distribution pattern of talc was not found. Concentra-

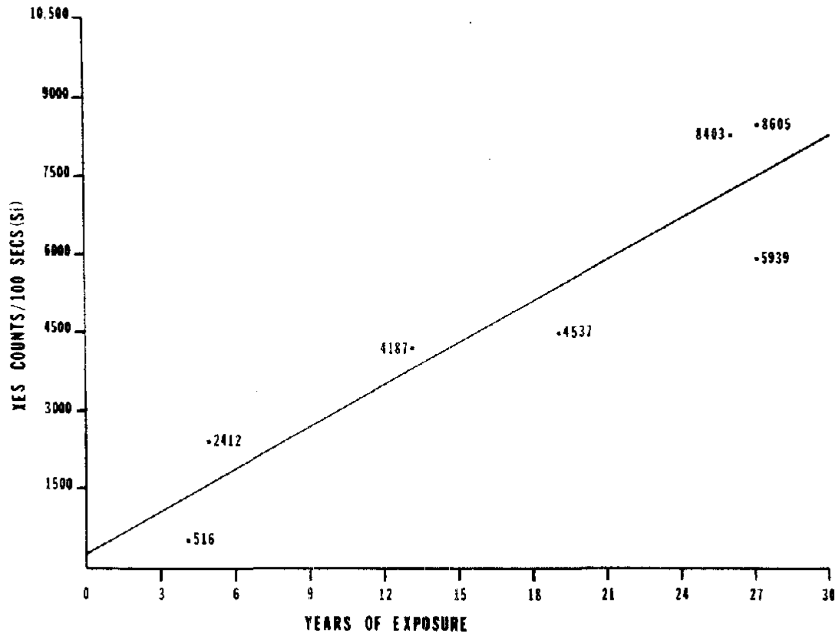

Figure 1. X-ray energy spectrometric analysis data obtained from silicon in the lung tissues in all seven cases. The X-ray counts for silicon are the mean from all the anatomical sites analyzed,

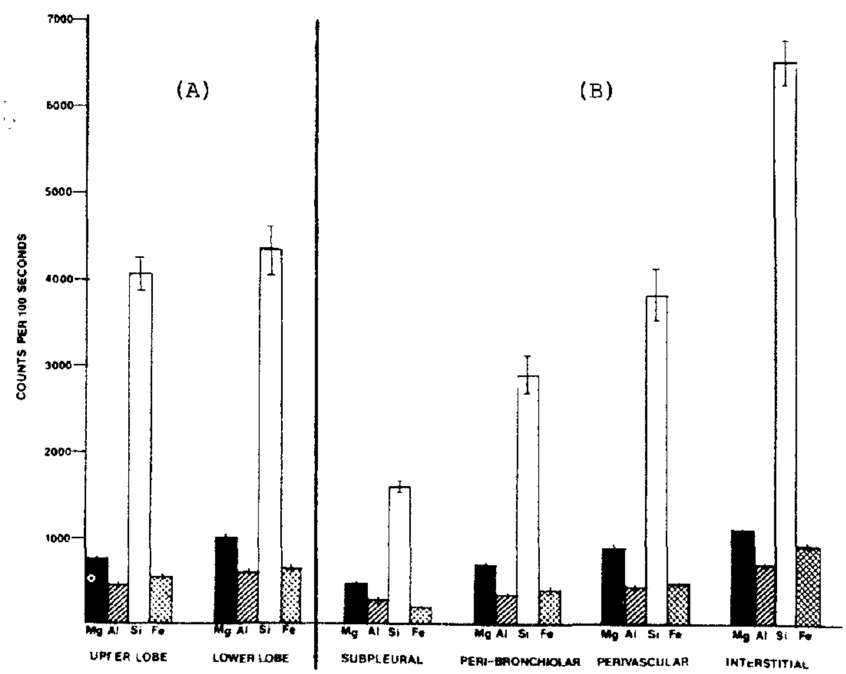

Figure 2. Semiquantitative X-ray energy spectrometric analysis showing the distribution of the major elements in anatomical sites of the left lung of one case. (A) describes the averages of element concentrations in the lobes of the lung and (B) describes the levels in the individual tissues. A significant difference in the lobar distribution pattern of talc was found.

tions of elements tended to be highest in the interstitial and perivascular lesions.

	Mg per 100 g. freeze dried tissue		
	Aluminium	Silicon	Iron
Case A	135 ± 31	360 ± 21	300 ± 13
Case B	70 ± 12	470 ± 14	430 ± 9
Case C	710 ± 218	3810 ± 280	448 ± 13
Normal controls	68 ± 25	68 ± 22	154 ± 47

5.2 INHALATION KINETICS EXPERIMENTAL ANIMAL DATA

Wehner et al. (1977B, 1979) studied the pulmonary deposition, translocation and clearance of inhaled talc baby powder in 10-week-old hamsters after receiving a single 2-hour, nose-only exposure to neutron-activated talc. Over a period of 4 months the hamsters were killed in groups of four. Lungs, liver, kidneys, ovaries, skinned carcass and 2-day and 4-day excreta were collected for γ-ray analysis. From 20 to 80 µg talc, an estimated 6-8% of the inhaled quantity, was deposited in the alveoli. The biological half-life of the talc deposited in the alveoli was 7-10 days. Alveolar clearance was essentially complete 4 months after exposure. No translocation of talc to liver, kidneys, ovaries or other parts of the body was found. Several micrograms of talc were found in the fecal samples.

Hanson et al. (1985) reported a method to determine lung burden in rats and mice that had been exposed to talc aerosols based on the Mg content of the talc. Thorough washing of lung tissue with 5% trichloroacetic acid effectively removed the endogenous acid soluble Mg present in the lungs. They suggested that inhaled dusts containing Mg contribute to the increase of insoluble Mg in the lung during the animal's lifetime. In their experiment they exposed Fischer-344 rats and B6C3F1 mice to increasing concentrations of respirable talc 6 h/d, 5 d/w for 4 weeks. The animals (five males and five females) from each exposure group were killed at the end of the exposure period and used for lung burden determination. The respirable talc had a mass aerodynamic diameter of 3.25 µm for the rats and 2.73 µm for the mice. The mean lung burdens for the rats were 77, 187 and 806 µg talc/g lung for exposures at 2.3, 4.3 and 17 mg talc/m^3, respectively. The mean lung burdens in mice were 114, 325 and 1150 µg talc/g lung for exposures to 2.2, 6.3 and 20.6 mg talc/m^3, respectively. The coefficient of variation for the lung burden of the different exposure groups ranged from 8 to 21%.

5.3 SUMMARY OF INHALATION KINETICS

From the human and animal experimental data the following conclusions can be drawn:

- The deposition of talc after inhalation probably depends on the aerodynamic diameter of the particles.
- The biological half-life of talc in the alveoli must be estimated in days or weeks.
- Talc is not absorbed through the lung into the blood; no translocation of talc takes place to liver, kidneys, ovaries or other parts of the body.
- The lung burden of respirable talc particles is dependent on the level and duration of exposure.
- Distribution of silicon levels in the lung showed preferences in the interstitial tissues, followed by perivascular tisssue, peribronchial tissue and the least in subpleural tissue.
- There is a significant linear correlation between the mean silicon levels in the lung as determined by X-ray count, and the duration of exposure to respirable talc dust in man.

5.4 INGESTION KINETICS, ANIMAL DATA

Wehner et al. (1977C) concluded from their study that intestinal absorption of talc is negligible and could have contributed minimally to the body burden of talc. In their experiment, neutron activated talc was suspended in physiological saline and administered to six Syrian golden hamsters by gastric intubation. The hamsters were killed 24 h after gavage and the organs analysed for radioactivity. An average of approximately 3 mg talc was found in the tissues and excreta. Of this quantity, 75% was found in the faeces, 24% in the gut and 2% in the carcass. The -ray counts from the urine accounted for 0.09% of the total, which was thought to be caused by leaching of ^{60}Co from the talc with subsequent absorption.

6 EFFECTS

6.1 ANIMAL EXPERIMENTS

6.1.1 Irritation and sensitization

No data are available. It is speculated that acute exposure at high concentrations in air the substance caused more nuisance than irritation of the upper respiratory tract.

6.1.2 Acute toxicity

The LD_{50} of talc has not been established unequivocally. In most studies as cited by IARC (1987), no acute mortality was observed in several species of animals following administrations of high doses of talc by ingestion, inhalation or intratracheal, intrapleural, intraperitoneal or subcutaneous injection.

6.1.3 Toxicity in short- and long-term exposure

A summary of the studies is shown in Table 1.

The reports on experiments in which the animals were exposed by inhalation to cosmetic grade talc showed contradictory results. Wehner et al. (1979) exposed golden hamsters to 8 mg/m^3 baby powder talc with a mean mass aerodynamic diameter of 6 µm, for 3, 30 or 150 min/day, 5 day/week for 30 days, or 30 or 150 min/day for a maximal of 300 days, reported no effect on the bodyweight, survival, type, incidence or degree of histopathological changes of the lungs, trachea, larynx, liver, kidney, stomach, uterus, ovary or testis when compared to the control group. On the other hand Wagner et al. (1977) an reported increased incidence of lung fibrosis when rats were exposed to 10 mg/m^3 Italian cosmetics grade talc (in which 40% were of respirable dimentions) for 7.5 h/day, 5 days/week, for 3, 6 and 12 months. The incidence of fibrosis was even about the same as in animals exposed to chrysotile asbestos fibers with the same exposure protocol. The experimental material was Italian talc. The mineral sample used in this experiment was obtained from a shipment of talc material imported from a mine in Northern Italy. It was chosen for

Table 1: Short-term toxicity studies on animals exposed to talc.

Sort of animals	Mode of exposure	Levels and talc-grade	Effects	Comments	Reference
rats	inhalation 6 h/d, 6d/w, 9 mo	30-383 mg/m^3 (technical grade or pharmaceutical	None died as consequence of exposure.	No data on particle dimentions.	Bethge-Iwanska, cited by IARC (1987)
rats	inhalation 7.5 h/d, 5 d/w 3, 6 and 12 mo	10 mg/m^3 (Italian talc) 40% respirable	Incidence of fibrosis is the same as in rats exposed to chrysotile fibers.	For other data see carcinogenic effects.	Wagner et al. (1977)
golden hamsters	inhalation 3, 30 or 150 min/d, 5 d/w, 30 days or 30 or 150 min/d, max. 300 days	8 mg/m^3 (talc baby powder) MMAD=6µm	No effect on body weight survival, type, incidence or degree of histopathological changes.	Cosmetic-grade talc does not contain asbestos fibers.	Wehner et al. (1979)
hamsters	intra-tracheal instillation, single exposure. Observation 1-14 days.	0.15, 0.75 and 3.75 mg per 100 g animal (quartz <1%, no asbestos) MMAD=7.5 µm	One day after exposure, signs of pulmonary edema increased cell numbers broncheolar lavage Macrophage phagocytosis was inhibited.	Difficulties in the extrapolation of the dose into inhaled air concentration.	Beck et al. (1987)

rats	<u>intra-tracheal</u> instillation, 1-4 injections	25 mg total dose per animal (talc containing tremolite) Diameter 0.1-0.2 µm	Proliferative inflammation in smaller bronchi and bronchioles. With time converted into collagenous sear tissue.	- idem -	Gross et al. (1970)
rats	<u>intrapleural</u> inocculation, single exposure observation >2 yr.	20 mg per animal (Italian talc, cosmetic grade)	No relevant pathology of lungs. One rat had a adenoma in the lung.	- idem - For other data see carcinogenic effects.	Wagner et al. (1977)
rats	<u>intraperitoneal</u> implantation, single exposure. Examination after 2,4, 8,13,26 and 52 wk.	50 mg per animal (high purity commercial sample) Diameter 0.2-20 µm	Peritoneal adhesions and severe granulomatous reaction at wk 2.		Pelling and Evans (1986)
mice	<u>intravenous</u> injection, single exposure. Observation 462 days	Various concentrations, further not mentioned.	Pulmonary microthrombi the early phase. Then granuloma formation. Final stadium perivascular fibrosis.	The purity of talc is not known. Probably of medicinal grade.	Püschel and Schoof (1987)

for two reasons, first, because it has been used in Great Britain for over 50 years and secondly, because over 40% of the cosmetic grade talc used in Great Britain is obtained from this source.

The induction of fibrosis by cosmetic grade talc is substantiated by other experiments. Pelling and Evans (1986) performed intraperitoneal implantation of 50 mg high purity commercial talc with a mean particle size of approximately 2 µm with a range of 0.2-20 µm in rats, found a 100% incidence of focal lesions already at week 2 after implantation, shown as an extensive granulomatous peritonitis. This was maintained till wk 13. In the later stadium there was a collagenization of the granuloma. More recently Püschel and Schoof (1987) injected intraveneously various concentrations of medicinal grade talc into mice and observed them for 462 days. In the early phase they found pulmonary microthrombi consisting of platelets, fibers and aggregation of leucocyts adjacent to talc particles. The consecutive granuloma formation was mainly influenced by the activated macrophages. In the final stadium there was perivascular fibrosis.

That quartz- and asbestos-free talc dust is not an inert particle but has the capacity to be irritant to the mucous membrane of the respiratory tract is shown by the experiments performed by Beck et al. (1987). They instilled pure talc (quartz content of less than 1% and no fibrous material detected by scanning electron microscopy) intratracheally to hamsters at doses of 0.15, 0.75 and 3.75 mg per 100 g animal. The mass median aerodynamic diameter was 7.5 µm with 26% with mass <5 µm, and 3% mass between 1-3 µm. One day after exposure resulted in elevated enzym levels and cellular levels in the bronchoalveolar lavage fluid and pulmonary edema. Macrophage phagocytosis was also inhibited. The talc used in this experiment was acquired from Vermont, USA, which is known to be free of asbestiform minerals and crystalline silica.

The pathogenesis of the induction of fibrosis was studied in vitro by Davies et al. (1983) on mouse peritoneal macrophages. Seven talc specimens were used: five were typical cosmetic grade talc (Indian Finex, Italian 00000, micronised Italian 00000, Spanish SS and Australian West Side), a sixth specimen contains a high level of chlorite (French OXO) and the seventh contained amphiboles (Chinese Haichen). The mineralogical content was determined by X-ray defraction analysis and transmission electron microscopy. These talc specimens were compared with magnetite (a non-fibrogenic dust) and quartz (a fibrogenic dust). It was found that all seven talc specimens were cytotoxic toward macrophages, the release of LDH (lactate dehydrogenase) being significantly higher than in the magnetite-treated cultures. However, the talc specimens were found to be far less toxic than the quartz sample. Since most of the specimens contained very low levels of contaminating minerals the authors suggested that the major active constituent of the dust was the mineral talc.

From the acquired data it may be concluded that quartz- and asbestos-free talc dust is fibrogenic, which means that in inhalation exposure it may cause fibrosis of the lungs, as found in animal experiments. The concentrations which are used in these experiments indicate that at the level of 10 mg/m^3 with 40% in the respirable range may already induce these effects in rats, on the other hand hamsters exposed to 8 mg/m^3 baby powder talc with MMAD of 6 µm showed no histopathological changes.

6.1.4 Carcinogenicity

6.1.4.1 Inhalation exposure

Wagner et al. (1977, 1979) exposed Italian talc to Wistar rats with a mean respirable dust concentration of 10.8 mg/m^3, 7.5 h/d and 5d/w. 48 Animals were exposed for 3 mo, 24 animals for 6 mo and 24 animals for 12 mo. Ten days after the end of each exposure period some rats were sacrificed and there were also sacrifices 1 year later. The Italian talc was used for two reasons, first because it has been used in Great Britain for over 50 years and secondly because over 40% of the cosmetic grade talc used in Great Britain is obtained from this source. The results showed that no tumours occurred in the control group and there was one adenoma of the lung in the rats exposed to talc. In the talc exposed animals no malignant tumours were found. On the other hand a group of rats exposed to chrysotile with the same protocol resulted in 7 lung tumours, including one adenocarcinoma and one lymphosarcoma. The main features are that both Italian talc and chrysotile produced fibrosis of the lung tissue to a similar extent (see 6.1.3). No tumours were found in hamsters when exposed to baby powder talc, according to Wehner et al. (1979). In their experiment, groups of 50 male and 50 female Syrian golden hamsters were exposed to talc aerosol for 3, 30 or 150 min/d, 5d/w for 30 days or for 30 or 150 min/d either until they died naturally within 300 days. The mean concentration of respirable aerosol fraction was approximately 8 mg/m^3 and the MMAD was 6 µm. The animals were observed for the remainder of their life-span. The exposures had no effect on body weight, survival or type, incidence or degree of histopathologic changes in the exposed groups compared with sham-exposed controls.

6.1.4.2 Intracheal instillation

No respiratory tumours were found when hamsters were exposed by intratracheal instillations with pharmaceutical grade talc (Stenbäch and Rowland, 1978). In their experiment, 24 male and 24 female 6-7 wk old Syrian golden hamsters received 3 mg talc suspended in 0.2 ml saline intratracheally once weekly, in a total of 18 instillations. The observation period was about 120 weeks. The talc had a pharmaceutical grade purity, consisting of silicon 61.0-63.0%, magnesium 32-34% and other dusts 0.85-1.06%. The particle distribution was as follows: 93% < 25 µm, 86% <16 µm, 54% <10 µm, 26% <5 µm and 2.1% <1 µm. The results showed that talc alone failed to induce respiratory tumours, granulomas or mesothelial proliferations. Three benign lesions of the lung were found, which were mucoepidermoid lesions. Other tumours which were found were two forestomach papillomas, one thyroid adenoma and one adrenal cortex adenoma.

6.1.4.3 Intrapleural injection

Wagner et al. (1977) reported that no mesotheliomas were observed in rats when injected intrapleurally with talc. The dose was 20 mg talc per rat in a group of 48 rats, made up as a suspension in physiological saline with a concentration of 50 mg/ml. The talc was cosmetic grade Italian origin with an upper particle size of 70 μm and a mean particle size of 25 μm, it contained 92% talc mineral by weight together with 3% chlorite and 1% carbonate minerals, quartz was also found in the powder at approximately 0.5-1% level. After the single dose an observation period of more than two years was effected. The mean survival time was 655 days, compared to that of controls of 691 days. At the injection site granulomas were common and a small pulmonary adenoma was found in one rat which died 25 mo after injection.

6.1.4.4 Intraperitoneal administration

Özesmi et al. (1985) injected 40 Swiss albino mice with 20 mg commercial talc intraperitoneally. There are some discrepancies in the contents of this report. Although in the material and methods it was reported that animals which died before 9 mo had elapsed after injection were excluded, but in the results it was shown as death before 6 mo. Furthermore no specifications were given on the purity of the talc dust as well as its origin and particle size distribution. The results showed that from the remaining 24 animals (16 died before 6 mo) three mesotheliomas were found. In comparison, in the control group of the remaining 46 animals (9 died before 6 mo) also three mesotheliomas and one lymphoma were found. In the absence of essential data, no conlusions can be made from this experiment.

6.1.4.5 Intrabursal administration

Hamilton et al. (1984) studied the effect of talc on the rat ovary by intrabursal implantation. The talc preparation was from Italian origin (Italian 00000) at concentrations of 100 mg/ml in phosphate buffered saline. This preparation was composed of a heterogenously sized population of platey cristals with a size range of 0.3-14 μm; it contained no asbestos fibers as judged by electron microscope microanalysis. A total of 95 animals were involved in the experiment: at each time point 10 treated animals were examined at intervals of 1, 3, 6, 12 and 18 mo after treatment. The results showed no evidence of cellular atypia of mitotic activity in the nonpapillary areas of the surface epithelium of the injected ovaries and in no ovary was there any evidence of neoplasia.

6.1.4.6 Oral administration

An estimated dose of 100 mg/day cosmetic grade talc (Italian origin) was fed to 32 rats through their diet (Wagner et al., 1977). Feeding started in February 1973, when the rats were between 21 and 26 weeks old, and was carried out for 101 days in the following 5 months. Except when the doses were being administered the rats had access to the normal diet. At postmortem the abdominal organs were examined. The mean survivals from the start of the feeding were 614 days for talc as compared to 641 days for the control group. Abnormalities of the gut were found in only one rat, which had a leiomyosarcoma of the stomach. Other findings were an adrenal adenoma in a control rat and sarcomas of the uterus in two rats fed with talc.

6.1.4.7 Mutagenicity

There are very limited data on the mutagenicity and genotoxicity of talc dusts. The following data were reported by the IARC (1987): Talc was not mutagenic to Salmonella typhimurium TA 1530 or his G46 or to Saccharomyces cerevisiae D3 in vitro or in host-mediated assays in mice with a dose of 30-5000 mg/kg/b.w. Chromosomal aberrations were not induced in human W138 cells treated with talc at 2-200 µg/ml, and neither chromosomal aberrations nor dominant lethal mutations were induced in rats following oral administration of 30-5000 mg/kg/b.w.

6.1.5 Reproduction Toxicology

In an experiment by the Food and Drug Research Laboratories in 1973 (cited by IARC, 1987) no teratological effects were observed in hamsters, rats, mice and rabbits following oral administrations of talc. The doses used were 1600 mg/kg/b.w. to rats and mice on days 6-15 of gestation; 1200 mg/kg/b.w. per day to hamsters on days 6-10 of gestation; and 900 mg/kg/b.w. to rabbits on days 6-18 of gestation.

Table 2: Reports of cases with granulomatous reactions of the lungs induced by inhalation of cosmetic grade talc.

Case	Clinical picture	Cause associations	Reference
31 year old woman	- increasing shortness of breath - reduced vital capacity - X-ray: diffuse reticular density and hazy nodules - PA: small fibers and asbestos bodies - Diagnosis: granulomatous and fibrotic changes	Past 6 or 7 years exposed to talcum powder aerosols in a cosmetic factory.	Moskowitz (1970)
39 year old male	- X-ray: diffuse, nodular infiltrate in both lungs - PA: extensive intra-alveolar and interstitial deposits of talc	Job history possible exposure to French talc (pure talc). Family interviews showed excessive use of body talc.	Nam and Gracey (1972)
41 year old housewife	- complains of shortness of breath - X-ray: shadowing in the right apex - abnormal lung function tests - PA: numerous granulomata and fibrosis. Particles consistent with talc	Habit of dusting whole body with talc.	Wells et al. (1979)

58 year old woman	- X-ray: fine diffuse opacities - normal lung volumes - PA: intra-alveolar and interstitial granulomatous inflammation - foreign body characteristic of talc	In 10 years period using talcum powder two to three times a day.	Tukianen et al. (1984)
55 year old woman	- complains of dyspnoea - X-ray: diffuse nodular opacities - PA: small interstitial granulomas	Job of packing rubber balls and exposure to talc used as dusting agent	Tukianen et al. (1984)

6.2 OBSERVATIONS IN MAN

6.2.1 Case-reports

The first case of talc pneumoconiosis was reported in 1896 (Lockey, 1981). With the identification of silica and asbestiform minerals in certain talc deposits, three forms of talc pneumoconiosis have been described: talcoasbestosis, talcosilicosis and pure talcosis. Talcoasbestosis has been extensively documented in workers exposed to industrial grade talc contaminated with asbestiform minerals. Exposed workers reported symptoms of dyspnea and cough, with physical findings of diminished breath sounds, basilar crepita tions, clubbing and cyanosis. Lung function tests showed reduced FVC, FEV_1,total lung capacity and CO-diffusing capacity. Lung abnormalities were also shown in chest röntgenography. Talcosilicosis has been less documented and there is a paucity of data on the prevalence of pure talcosis. It may be concluded that the toxic effects of talc are dependent on the route, dose, duration of exposure and the properties of the talc involved.

Reports of cases with pulmonary granulomatous reactions suspected being induced by exposure to cosmetic grade talc through inhalation are summarized in Table 2. From these data it may be concluded that there exists a risk of acquiring pneumoconiosis in excessive exposure to cosmetic grade talc. Estimation of the dose to induce these aberrations is almost impossible. There seems to be a pattern in the clinical picture of the patients, with complains of shortness of breath as the first signs. Lung function tests showed a normal picture in the first stadium with possibly a lowering of the diffusing capacity. In the later phase there was a diffuse nodular infiltration involving both lungs. Pathologic examination showed numerous granulomata and extensive fibrosis. The granulomata mostly exhibited no necrosis, but multinucleated giant cells with talc particles on further analysis.

Cases of pneumoconiosis were also reported in workers employed in the mining and milling of talc that contained minimal amounts of crystalline silica and asbestiform minerals (Vallyathan and Craighead, 1981). The lungs exhibited varying degrees of fibrosis, located either adjacent to the vessels and bronchi or diffusely. Semiquantitative estimation of talc in the lung tissue indicated that the extent of the pulmonary lesions corresponds to its concentrations in the tissue. It is evident that relatively short-term exposure results in the development of focal lesions, primarily located adjacent to small airways and vessels. On the other hand, prolonged exposure to high concentrations of dust is associated with diffuse deposits of fibrotic tissue in which variable numbers of multinucleated giant cells are found.

A case of pleural mesothelioma was reported by Barnes and Rogers (1984) in a 44 year old woman in Australia. She was a lifelong non-smoker. Her sole employment was as a process worker in an artificial jewelry factory for 12 years. Part of her duty was dusting with industrial grade talc as a separation agent in a centrifugal casting process by means of rubber moulds. No obvious exposure to asbestos could be obtained from examination of the occupational history, yet examination of the lung tissue revealed the presence of elevated levels of amosite. Barz and Beck (1983) in Germany also reported a case of pleural mesothelioma, asbestosis and silicosis in a 69 year old man after a long time exposure to industrial grade talc dust. The patient had an occupational history as "Kernmacher" for 40 years, in which job the talc had been used to prevent clinging of the mixture to the form. In this case the first exposure to talc occurred about 55 years before death.

Cases are reported of lung aberrations induced by extraordinary administration of talc. O'Connor et al. (1988) reported a case of pulmonary talc granulomatosis in a 32 year old man with AIDS. Transbronchial biopsy showed granulomatous inflammation with foreign materials consistent with talc. The man was an intravenous drug abuser and it was suspected that the talc entered the body through this way. About the same findings were also reported by Farber et al. (1982). In four of six patients with pulmonary talc granulomatosis secondary to the intravenous injection of suspended, crushed tablets, they found talc crystals in the bronchoalveolar lavage. Other effects were also reported as caused by intravenous injection of talc, such as ocular manifestations (Carman, 1985) and talc granulomatosis of the skin (Apple et al., 1985). A case of unusual intestinal talcosis was reported by Anani et al. (1987) in a 46 year old man who had taken tablets containing talc over a period of 28 months.

6.2.2 Case-control studies

Hartge et al. (1983) found no overall association between talc use and risk of ovarian cancer. They performed a case-control study of epithelial ovarian cancer conducted in 1974 to 1977 in the Washington DC area. The cases were 197 women with pathologically confirmed primary epithelial ovarian cancers treated in participating hospitals. The controls were 197 women treated at the same hospitals for conditions other than gynaecologic, psychiatric, malignant disease or pregnancy. They were matched for age, race and hospital. The estimated relative risk to talc users was 0.7 (95% confidence interval = 0.4-1.1). Cramer et al. (1982) also performed a case-control study on females in the Boston area to study the association between ovarian cancer and talc. The study population was 215 white females with epithelial ovarian cancers and 215 control women from the general population matched for age, race and residence. Of the other cases 42.8% regularly used talc either as a dusting powder on the perineum or on sanitary napkins compared with 28.4% of the controls. Adjusted for parity and menopausal status, this difference yielded a relative risk of 1.92 ($P<0.003$; 95% CI=1.27-2.89) for ovarian cancer. Women who regularly engaged in both practices had a adjusted relative risk of 3.28 ($P<0.001$, 95% CI=1.68-6.49) compared to women without exposure.

It may be concluded that the question of the induction of ovarian cancer by extensive use of talc is still ambiguous. The results of the study from Hartge et al. (1983) are contradictory to those of Cramer et al. (1982). Although they have almost the same number of cases and controls, a big difference lays on the specifications of the control group. The former used patients hospitalized in the same hospital and the latter used healthy women from the general population. Some bias in the motivation for participation and answering the questionnaire should be expected from the latter.

Table 3: Cross-sectional studies of workers occupationally exposed to talc dust (E = exposed group; C = control group).

Number workers	Occupation and/or type of plant	Specifics of talc-dust	Duration of exposure	Effects on the lungs	Comments	Reference
E = 202 C = 101 (same SES)	grinding of soapstone	industrial grade, no asbestos. Less than 1% free silica.	4.28 mean years of exposure	Ventilatory capacities decline with increase in the duration of exposure. Significant after 5 years of exposure.	No data on levels of exposure.	Damodar et al. (1983) India
- " -	- " -	- " -	- " -	More symptoms of the respiratory system. More workers with nasal and pharyngial congestion.	- " -	Damodar and Agarwal (1985) India
E = 80 C = 189 (same plants)	rubber industry	industrial grade talc, non fibrous. less than 1% free silica. Asbestos <2f/ml. Mean respirable dust: 0.50-3.55 mg/m^3	mean of employment 15.9 y (E) 13.4 y (C) Dust years = 8.9 (mean)	Higher prevalence of COLD. Decreased lung function. Increased respiratory morbidity. X-ray: no signs of talc pneumoconiosis.	Majority of jobs under under 1 mg $dust/m^3$. No differences between E and C in smoking. Suggestion for a TLV of 0.25 mg/m^3 respirable talc dust. For more information see 6.2.3.	Fine et al. (1976) USA

121 male workers (E) control group are potash workers (n=?)	miners and millers	talc containing tremolite and anthophyllite. Range of respirable dust: 0.23-2.96 mg/m^3. Fibers in mine 38% anthophyllite 19% tremolite 3% chrysotile	10.2 mean years of exposure	Decreased pulmonary function. Increased prevalence of pleural calcification and pneumoconiosis.	Decreased FEV_1 and FVC was associated with with exposure to respirable dust and asbestiform fibers. It should be noted that the exposure to dust and free silica is in control group is higher than exposed group.	Gamble et al. (1979) USA
39 workers (E) 41 workers (C) (same area, sex, age range)	miners and millers	commercial talc containing tremolite and anthophyllite. Last data of mean dust count = range of 6-62 mppcf.	mean 16.2 years (range 11-22 y)	Only 1 individual in group showed pneumoconiosis on X-ray. On symptomatology, only higher incidence of dyspnoea.	Crude method of air samples collection by midget impinger and fiber count.	Kleinfeld et al. (1973) USA

6.2.3 Cross-sectional studies of workers

A summary of cross-sectional studies of workers occupationally exposed to industrial grade talc is presented in Table 3.

The study as reported by Fine et al (1976) is of interest and will be presented further in this document. Pulmonary function tests, chest X-ray and respiratory questionnaires were administered to 80 talc workers and 189 non-exposed rubber workers from three rubber tire manufacturing plants. The exposure to talc was evaluated by respirable mass sampling using PAS. Standard asbestos counting was utilized and the free silica was analyzed by infra red technique. In one plant the average mass respirable dust concentrations ranged from 0.51 to 3.55 mg/m^3 and in the other plant 0.47-1.41 mg/m^3. The exposure for the majority of the jobs was under 1 mg/m^3. The free silica concentration contained less than 1% and the asbestos fibers less than 2 f/ml. The distribution of years of cigarette smoking between the two groups was comparable, as well as the lengths of employment. The "dust" years for the exposed group was 8.9 ± 6.5 years. Socioeconomic and ethnic factors differed not very much. In the exposed group there was a high prevalence of symptoms associated with mucous hypersecretion and chronic bronchitis. There were more workers with history of COLD in the exposed group, but no symptoms of recurrent pulmonary infections. There is a suggestion that talc and smoking interact to cause the increased prevalence of wheezing. Pulmonary function tests performed only on white workers over 24 years old showed that talc workers had lower FVC, lower residual FEV_1, and lower FEV_1/FVC ratio, despite being younger and smoked less cigarettes than the control group. A multiple regression of the data of the talc workers showed that the predictors of FEV_1 were age, height, years of cigarette smoking and years of exposure to talc. It suggested that for each year of exposure to talc the worker suffered a 26 ml loss of FEV_1 in excess of the related age and cigarette smoking. The authors suggested that a level of 0.50 mg/m^3 should limit the average loss of FEV_1 over an entire working life-time to 250-500 ml among talc workers. It should be pointed out that a drawback on this study is that exposure to agents in this kind of industry is not only restricted to talc dusts, but other chemical agents which have an effect on the respiratory system may be present as well.

6.2.4 Longitudinal studies of workers

Wegman et al. (1982) performed a one-year follow-up study on a group of miners and millers currently employed by three talc companies in Vermont, US. From a start of 116 subjects, whose age were 25 or older, it ended with 103 subjects. Information on exposure was attained from three sources: data from former times when monitoring was performed by midget impinger, the present method by personal sampling measuring respirable mass samples and the third was historical information from each company. For the job exposure assignments the "talc years" was calculated. The results of analysis showed that the talc was found to be free from silica and asbestos. Exposure levels were found to be below 3.0 mg/m^3 and the geometric mean of the exposure was 1.8 mg/m^3 of respirable dust. The lung function test data showed that the mean observed/predicted FVC was not changed but significant reduction occurred for FEV_1 and MMEF. When exposure to talc was considered, years of employment and "talc years" were significantly related with decreasing FEV_1/FVC and MMEF, but not with FVC or FEV_1. The same effects were seen even after stratification for the smoking habits. Chest radiography examinations exhibited that 12 subjects had small round or irregular opacities (perfusion 1/0 or greater); five of them had never smoked. Clinical symptoms indicated that both pack-years and exposure duration to talc showed a weak correlation with symptoms of cough and phlegm.

From this study it may be concluded that at the level of exposure of 1.8 mg/m^3 respirable talc dust, which is free from silica and asbestos, aberrations to the lungfunctions, can already occur.

It should be reminded that there are some questionable detriments in this study. The omission of a standardised control group weakens the overall results of this study, although the authors try to accomodate this by using the predicted values from a standard population, since no regional differences are found.

6.2.5 Retrospective-cohort mortality studies

A summary of these studies is presented in Table 4. As can be seen from these data, one of the most difficult consideration in this kind of studies, in which effects on the lungs should be the end-point, is the unavailability of data on the smoking habits of the studied population. The risk that the smoking habits between the "observed" group will differ with the "expected" group should be taken into consideration when reading the result of these studies. Another matter to keep in mind is that workers probably are not only exposed to pure talc dust but also to other contaminants which are incorporated into the talc since its extraction from the mines. These are mostly dependent on the origin/place where the mining operation is taking place. Most of the talc reported in this table are probably from the industrial grade talc or crude talc dust, and the majority originated from the talc plants in New York. An analysis of samples of mined and milled talc from New York yielded the following concentrations of minerals: talc, 12-50%; tremolite, 30-55%; anthophyllite, 3-35%; serpentine, 1-8%; calcite, <1-4%; and quartz, <0.1-20% (IARC, 1987). Most of the studies in this table 4 reported increased risks for cancer of the respiratory tract and of the lungs. It is not possible to trace back the original agent which may have been the cause of the reported effects. The only conclusion which may be forwarded is that in such situations in which workers are exposed to industrial grade talc including itsoriginal contaminants, there exists a risk of attaining cancer of the respiratory tract and the lungs.

There is only one study in which the workers are exposed to cosmeticgrade talc, and that is from Rubino et al. (1976). In this study data were collected for each worker who began work in the years between 1921 and 1950 and who has been employed for at least one year in the talc mine and mill in Piedmont, Italy. The studied population consisted of 1514 miners and 478 millers and an age-matched control group was taken from the population of a small town, 38 miles away from the plant, with similar ethnic and social economic status. As an exposure index, the cumulative dust exposure for each man was estimated and expressed as mppcf/years. The follow-up was 88.9% for miners and 91.6% for millers.

Table 4:A summary of retrospective cohort mortality studies of workers exposed to talc dust, with special reference for diseases of the lungs.

Factories or occupations (country)	Number of cohort	Exposure specifics	Years of observation	Source of expected number	Mortality	Comments	Reference
mining, grinding and processing of talc (USSR)	no data	talc with no tremolite, 0.2-1.6% quartz	1949-1975	population from the same town	RR for lung cancer, for male 4.5 ($P<0.02$) for female 9.3 (N.S.)	This study lacks in the presentation of data. No correction for smoking habits.	Katsnelson and Mokronosova (1979)
"talc workers" (USA)	260	exposure duration ≥15 years for commercial talc admixed with tremolite and anthophyllite	1940-1969	national deaths among white men	PMR for cancer of the lung and pleura about 4 times that expected (O/E=12.0/3.7). Prominent at age-group of 60-79 years old.	Autopsy records only in 38 of 108 total deaths. No clear statistical analysis.	Kleinfeld et al. (1974)
talc plant in New york (USA)	741 male and female (white) followed-up only 705 male	Talc containing tremolite. Duration of employment has a mean of 4.7 years.	1947-1978	national death rates	SMR significantly increased for: - all cancer 165 (108-242) - respiratory system cancer 246 (131-420) - lung cancer 240 (124-419) - all nonneoplastic respiratory disease 236 (113-435)	No data on levels of exposure. Excess mortality to lung cancer concentrated on employees who were employed less than one year. No correction for smoking habits.	Lamm et al. (1988)

talc miners and millers in Piedmont (Italy)	1514 miners and 478 millers	cumulative exposure calculated as mppcf/ year. Dust count in 1949-1955:12-602 mppcf 1956-1960: 8- 49 mppcf 1961-1965: 4- 13 mppcf Fiber count ≤ 0.01 f/ml	(1921-1950)-1974	population of town with similar ethnic and SES characteristics	Significant O/E ratio found for: - respiratory disease 140/101.8 (1.38) - silicosis 62/30.9 (2.01) - silico-tuberculosis 18/9.1 (1.98) Not for neoplasms.	No correction for smoking habits. In 1979 study was repeated using Expected Deaths Rate of Italian male population. No increased SMR for neoplasm.	Rubino et al. (1976)
Vermont talc industry (USA) miners and millers	392 male Caucasians, at least one year	Talcs in mines and mills similar composition. Free silica <0.25%. No asbestos fibers. Levels of exposure in the past probably >20 mppcf.	(1940-1969)-1975	Rates in Vermont and US male population	Only significant for mortality due to non-malignant respiratory disease (O/E=11/ 1.79). Respiratory cancer significant only in miners (O/E=5/1.15).	No smoking habits data. One of the miners probably contaminated with tremolite.	Selevan et al (1979)
talc miners and millers in New York (USA)	655 white male workers	No specifications on the talc.	1948-1978	US white male population	Increased SMR for cancer of respiratory system (163) and lung (157), but both not significant.	Data of smoking habits not available. No data on levels of exposure.	Stille and Tabershaw (1982)

pottery workers at three plants (USA)	2055 white men, employed at least 1 year	Exposed to silica and talc (non-asbestiform dust. Tremolitic talc was used until 1976. No airborne levels were available.	(1939-1966)-1981	US white male population	Significant increased SMR for lung cancer 1.43 (O/E=52/36.3) and non-malignant respiratory disease of 1.73 (O/E=64/37.0).	No smoking habits data. Mortality from lung cancer rose with increasing duration of exposure to non-fibrous talc (but high silica).	Thomas and Stewart (1987)

No smoking data were available for the exposed as well as the control groups. The results showed that the overall mortality of talc miners and millers is significantly lower than expected. Subdivision of the mortality by cause showed that death from all respiratory diseases is significantly higher than expected (O/E = 140/101.8). Further analysis exhibited the excess mortality to be due to the high incidence of pneumoconiosis with or without tuberculosis. The ratio's for the mortalities due to cancer of the respiratory tract and the lungs were lower than expected (lung, bronchus and trachea O/E=9/19.7). The cosmetic grade talc to which the miners were exposed consists of platy talc free of asbestos fibers but containing 5% of silica dust which arises from the footwall rock in the mine. The talc dust to which the millers were exposed was at least 90% pure talc, free from asbestos but containing 0.5% by weight of free silica and 3-4% by weight of chlorite and 1-2% by weight of carbonate (Hildick-Smith, 1975).

From the results of this study it may be concluded that there are no indications that the risk of attaining cancer of the respiratory tract and the lungs in workers exposed to cosmetic grade talc is lower than in the not exposed population. Since this is found in only one study it certainly needs confirmation.

6.3 SUMMARY OF THE EFFECTS

6.3.1 Animal data

- From the experiments to study the toxicity of talc it may be concluded that quartz- and asbestos-free talc dust is fibrogenic, which means that in the inhalation exposure it may cause fibrosis of the lung tissue. The concentration which may induce this effect is estimated at 10 mg/m^3 with 40% in the respirable range, for rats. But on the other hand hamsters exposed to 8 mg/m^3 baby powder talc with MMAD of 6 µm showed no histopathological changes of the lungs.
- Long-term inhalation studies on rats and hamsters showed that cosmetic grade talc does not induce malignant tumours of the lungs as well as other organs. "Pharmaceutical" grade talc given by way of 18 intratracheal instillations to hamsters and observed for 120 weeks also

failed to induce respiratory tumours, granulomas or mesothelial proliferations. Also no malignant tumours were found when cosmetic grade talc was administered by intrapleural injection in a single dose and observed for two years. In one experiment in which mice were injected intraperitoneally with talc the results showed an unusual outcome of increased incidence of mesotheliomia in the exposed as well as in the control group. Furthermore the authors did not specify the purity or grade of the talc being used. In an experiment in which cosmetic grade talc was given by way of intrabursal administration there was no evidence of aberrations in the nonpapillary areas of the surface epithelium of the injected ovaries and in no ovaries was there any evidence of neoplasia. Cosmetic grade talc given by oral administration to rats for 101 days showed that only one rat of the exposed group of 32 rats had a leiomyosarcoma of the stomach. Other findings were one adrenal adenoma in a control rat and sarcomas of the uterus in two rats fed with talc.

- Talc is not mutagenic and it does not induce chromosomal aberrations.
- Talc is not teratogenic by oral administration; no data are available by inhalation exposure.

6.3.2 Human data

- Most case reports described the lungs as the target organ in workers occupationally exposed to talc dust. The most common disease is talc pneumoconiosis. Depending on the contents of the dust three forms of this disease have been recognized: talcoasbestosis, talcosilicosis and pure talcosis.

Granulomatous reactions of the lungs have been reported in cases exposed to cosmetic grade talc. In these instances it is impossible to estimate the dose of the talc dust in the inhaled air which induce these aberrations. There are indications that accumulation of talc in the lung tisssue may play an important role in the pathogenesis. It is found that by semiquantitative estimation of the talc in lung tissue the extent of the pulmonary lesions corresponded with the talc concentration in the tissue. Two cases of pleural mesothelioma in workers with exposure to industrial grade talc, probably contaminated with asbestos, are reported.

- Two case-control studies to examine the relationship between ovarian cancer and extensive use of cosmetic grade talc for hygienic purposes, produce contradictory results. The difference in the choice of control groups may be the cause of this contradiction.
- There are a number of cross-sectional studies of workers occupationally exposed to talc dust. Most of them showed effects on the lungs as shown in increased symptoms of the respiratory system and decreased lung functions. In one well performed study it is shown that workers exposed to talc, with free silica content of less than 1% and a level of asbestos fibers of less than 2 f/ml (cosmetic grade?), a high prevalence of workers with symptoms of mucus hypersecretion and chronic bronchitis was found. A decrease of the lung function was also found; it was estimated that for each year of exposure to talc the worker suffered a loss of 26 ml of FEV_1 in excess of the related age and cigarette smoking. The authors suggested that a level of 0.50 mg/m^3 should limit the average loss of FEV_1 over an entire working life to 250-500 ml among the talc workers.
- There is one longitudinal study on workers exposed to talc free from silica and asbestos (cosmetic grade). They were followed-up for one year. The exposure levels to talc dust have a geometric mean of 1.8 mg/m^3 of respirable dust. A significant relationship was found between the years of employment and "talc years" with decreasing lung function tests (FEV_1/FVC ratio and MMEF). It may be concluded that at 1.8 mg/m^3 respirable dust already induce effects.
- There are various retrospective-cohort mortality studies. Most of them reported the mortality of workers which had been exposed to industrial grade talc or crude talc dust in the mines. One of the confounding factors in this case is that the talc dust contaminants depended on the original mining area. The talc dust from mines in New York is well known to be contaminated with free silica and the amphiboles, tremolite and anthophyllite. In these studies an increased mortality due to cancer of the respiratory tract and the lungs is found.

  On the other hand in a study in which the workers had been exposed to cosmetic grade talc, in a talc plant in Italy, no increased mortality due to cancer was found. Otherwise they found a higher incidence of pneumoconiosis with or without tuberculosis among the exposed workers.

7 PREVIOUS EVALUATION BY INTERNATIONAL BODIES

The American Conference of Governmental Industrial Hygienists (ACGIH) has an evaluation for their recommendations for the threshold limit value of talc dust.

The following TLV's were recommended: for talc containing no asbestos fibers TLV-TWA of 2 mg/m^3, respirable dust for talc containing asbestos fibers, use asbestos TLV's, however should not exceed 2mg/m^3, respirable dust.

After a review of data of 3.5 pages they came to the conclusion that the dust of non-fibrous talc, consisting almost entirely of platiform talc crystals, and containing no asbestos, carries a relatively small respiratory hazard that must be controlled. The degree to which controls should be applied to talc dust should depend upon its asbestos content.

There is no direct quantitative rationalization why the concentration of 2 mg/m^3 has been used as standard for talc containing no asbestos fibers. The most reasonable assumption after looking at their data is that it is probably attained from animal experimental data, in which hamsters were exposed to baby powder at levels of 9.8 or 8.1 mg/m^3 for totals of 1.5 hours, 15 hours or 75 hours over a 30 days period and another group was exposed for 30 or 150 minutes per day for 300 days. Results showed no significant lesions on the lungs after they were allowed to live out their lives.

The DFG (Federal Republic of Germany) recommended a MAK level for talc dust (free from asbest fibers) of 2 mg/m^3 (as fine dust), t.w.a.-8 h (the finalization was done at 7-7-1987). The assessment of the OEL was performed for the prevention of pneumoconiosis, lung functional changes and fibrosis of the lungs. The estimated avarage of exposure which induces these effects was 0.7 mg/m^3 fine dust. It is therefore that the following comments were made: "Wegen der gegenwärtigen Bestreibungen zur einheitlichen Verwendung einer Beurteilungszeit von 8 Stunden wird diese Regelung gegenüber der gleichwertigen Festlegung eines halb so grossen MAK-Wertes mit Jahresbezug bevorzugt".

8 EVALUATION OF HUMAN HEALTH RISKS

8.1 GROUPS AT RISK

No specific groups at extra risk are mentioned in the literature. Taking into account the lungs as the target organ in inhalation exposure to talc, it may be presumed that people suffering from chronic non specific lung diseases and people with acquired hyperreactivity of the airways should be classified as groups at extra risk.

8.2 ASSESSMENT OF HEALTH RISK

An assessment of exposure to talc dust should begin with understanding the characterisitics of talc. Talc as a pure chemical compound is defined as hydrated magnesium silicate. It occurs in sheets which readily cleave and break down to form flat, flaky plates and, to a lesser degree, short rolled sheets. A variety of elements such as nickel and iron may be included in the talc particle lattice but are so bound within the particle that they are not free to exert any biological actions (Hildick-Smith, 1970). The purity and physical form of any sample of talc dust are directly related to the source of the talc and to the minerals found in the ore body from which it is mined.

In the spectrum of biological effects induced by talc dusts, the purity and existing contaminants play an important role on the outcome. It is therefore imperative to distinguish two different groups of talc dust:

(1) cosmetic grade talc is a talc which is mined from selected talc deposits and can be defined as containing at least 90% mineral talc that is free of detectable amounts of asbestos, but may be associated with limited amounts of other minerals (Lockey, 1981).

(2) Industrial grade talc is a talc which is usually composed of talc combined with a variety of mineral dusts to provide the desired physical properties. Industrial talcs can have a low mineral talc content and may contain free silica and other minerals and can contain asbestos. It is therefore imperative that to determine the possible effect

of exposure to industrial grade talc dusts on health, it is important to identify the amount and composition of the talc dusts in the working environment.

Another important aspect in the evaluation of exposure is the particle size distribution of the talc dust. It may vary in relation to the process used to make the powder, with common cosmetic talcs having particles ranging between 0.3 to 50 µm (Hildick-Smith, 1975). It is shown in the kinetics that the deposition after inhalation is probably dependent on the aerodynamic diameter of the particles.

From short-term toxicity studies in experimental animals exposed by inhalation it was shown that quartz- and asbestos-free talc dust is fibrogenic, causing fibrosis of the lungs. The concentrations which are used in these experiments indicate that exposure at the level of 10 mg/m^3 with 40% in the respirable range may already induce these effects in rats, on the other hand hamsters exposed to 8 mg/m^3 "baby powder" talc with MMAD of 6 µm showed no histopathological changes. This may be due to the relatively high MMAD in comparison to the first study. Human case reports also described the lungs as the target organ in exposure to talc dusts. The most common disease is talc pneumoconiosis. Granulomatous reaction of the lungs have been reported in cases exposed to cosmetic grade talc, although it is impossible to estimate the level of exposure.

Long-term carcinogenicity studies on experimental animals exposed by inhalation showed that cosmetic grade talc is not carcinogenic. The IARC concluded that talc is not mutagenic.

From a cross-sectional study on workers in three rubber tire manufacturing plants occupationally exposed to talc dusts it was shown that one of the first signs of anomalies of the lungs was decrease of the lung functions. In this study in which workers were exposed to talc dusts with free-silica content of less than 1% and asbestos fibers of less than 2 f/ml, it was estimated that for each year of exposure to talc the worker suffered a decrement of 26 ml of FEV_1 in excess of the related age and cigarette smoking. Bringing in relation with the levels of talc dusts in air, the authors extrapolated that exposure to 0.50 mg/m^3 would limit the average loss of FEV_1 over the entire working life to 250-500 ml among the workers. We may regard this level as the Minimal Adverse Effect Level (MAEL) for exposure to respirable talc dust. It should be reminded that in this kind of industry, exposure to other chemical agents may also play a role in the development of toxicity to the respiratory tract.

In a mixed longitudinal-cross sectional study of one-year of workers occupationally exposed to talc, a significant relationship was found between the duration of exposure with decreasing lung functions as seen in the FEV_1/FVC ratio and MMEF. From this experiment it may be concluded that at a geometric mean of 1.8 mg/m^3 respirable dust there still are found effects on the lung function, which may be classified as Minimal Adverse Effect Level (MAEL). A drawback in this study is the omission of a standardised control group. The authors tried to accomodate this by using the predicted values from a standard population, since no regional differences were found.

Retrospective cohort studies on workers occupationally exposed to cosmetic grade talc indicated no increased mortality due to malignancy, on the other hand exposure to industrial grade talc or crude talc dust in the mines at specific locations in which contaminations with asbestos fibers were known, showed increased mortality due to cancer of the respiratory tract and the lungs without any possibility to postulate a quantitated relationship between exposure and risk by, among other things, possible interference with the effects of unknown smoking habits.

After assessing all accumulated data a health-based recommended-occupational exposure limit for talc dust can be proposed: For cosmetic grade talc, a level of 0.25 mg/m^3 t.w.a. 8 h, in the respirable range, is proposed. This level should provide sufficient margin of safety (2-7) to the MAEL's as found in the cross-sectional (0.50 mg/m^3) and the mixed longitudinal-cross sectional studies (1.9 mg/m^3).

For industrial grade talc containing free silica and asbestos fibers, the regulations for asbestos and free silica should be applied.

9 HEALTH-BASED RECOMMENDED OCCUPATIONAL EXPOSURE LIMITS

Cosmetic and Industrial grade talc, free from silica and asbestos fibers*	0.25 mg/m^3 t.w.a. 8 hours, respirable range
Industrial grade talc, containing silica and asbestos fibers	should follow the rules for occupational exposure to asbestos and free silica

* Industrial grade talc dusts free from silica quartz and asbestos fibers is defined as dusts containing none whatsoever of these contaminants.

10 RECOMMENDATIONS FOR RESEARCH

- Longitudinal studies on workers occupationally exposed to talc dusts are recommended with priority of finding a dose-response relationship on the effects of the lungs, special attention should be paid to the characterizations of the dusts.

- More understanding in the animal experiment as extrapolation model to human exposure needed verification. More so in case of respirable particles, since it is probably different between the small animals and human, depending on the anatomy and mechanic of the lungs.

- Interactions between substances with the same target organs needed clarification. Talc dusts as well as free-silica and asbestos in this case, has the same target organ, the lungs.

11 REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists) (1986). Documentation of the threshold limit values and biological exposure indices: Talc, Fifth edition. Cincinnati, Ohio, pp. 550-553

Anani,P.A., C.Ribaux and D.Gardiol (1987). Unusual intestinal talcosis. Amer. J. Surg. Pathol. 11, 890-894

Apple,J.S., S.Martinex, S.McAllister and A.H.Tatum (1985). Case report 330. Skeletal Radiol. 14, 291-294

Bachani,D. and D.Agarwal (1985). Impact of talc dust on the respiratory system of working population. J. Indian Med. Ass. 83, 41-43

Barnes,R. and A.J.Rogers (1984). Unexpected occupational exposure to asbestos. Med. J. Australia 140, 488-490

Barz,H. and B.Beck (1983). Pleuramesotheliom, Asbestose und Silikose nach langjährige Talkum Exposition. Z. Erkrank. Atm.-Org. 160, 167-172

Beck,B.D. H.A.Feldman, J.D.Brain et al. (1987).The pulmonary toxicity of talc and granite dust as estimated from an in vivo hamster bioassay. Toxicol. Appl. Pharmacol. 87, 222-234

Boundy, M.G., K.Gold, K.P.Martin Jr. et al. (1979). Occupational exposures to non-asbestiform talc in Vermont. In: Dust and disease, Lemen, R. and J.M. Dement (eds.), Patholtox publishers Inc., Illinois, pp 365-378

Brown,D.P., J.J.Beumont and J.M.Dement (1983). The toxicity of Upstate New York talc (let. to ed.). J. Occup. Med. 25, 178-179

Carman,C.R. (1985). Talc retinopathy. J. Amer. Optometric Ass. 56, 129-130

Cramer,D.W., W.R.Welch, R.E.Scullly and C.A.Wojciéchowski (1982). Ovarian cancer and talc, a case-control study. Cancer 50, 372-376

Damodar,D.A. and P.N. Sharma (1983). Changes in ventilatory capacities due to exposure to talc dust. Indian J. Chest Dis. Allied Sci. 25, 21-24

Davies,R., J.W.Skidmore, D.M.Griffiths and C.B.Moncrief (1983). Cytotoxicity of talc for macrophages in vitro. Fd. Chem. Toxicol. 21, 201-207

Delaude,A. (1985). Les pneumoconiosis dues au talc français. Bull. Acad. Nat. Méd. 169, 581-585

Dement,J.M. and R.D.Zumwalde (1979). Occupational exposures to talcs containing asbestiform minerals. In: Dust and disease, Lemen, R. and J.M. Dement (eds.) Pathotox. publishers Inc., Illinois, pp 287-305

Farber,H.W., R.P.Fairman and F.L.Glauser (1982). Talc granulomatosis: Laboratory findings similar to sarcoidosis. Am. Rev. Respir. Dis. 125, 258-261

Feigin,D.S. (1986). Talc: understanding its manifestations in the chest. Am. J. Rontgenology 146, 295-301

Feigin,D.S. (1986). Talc: its manifestations in the chest (let.) Am. J. Rontgenology 147, 439

Fine, L.J., J.M.Peters, W.A.Burgess and L.J.di Bazardinis (1976). Studies of respiratory morbidity in rubber workers. Arch. Environ. Health 31, 195-200

Gamble,J.R., W.Fellner and M.J.Dimeo (1979). An epidemiologic study of a group of talc workers. Am. Rev. Respir. Dis. 119, 741-753

Gross,P., R.T.P.de Treville, L.J.Cralley et al. (1970). The pulmonary response to fibrous dusts of diverse compositions. Am. Ind.Hyg. Ass. J. 31, 125-132

Hamilton,T.C., H.Fox, C.H.Buckley et al. (1984). Effects of talc on the rat ovary. Br. J. Exp. Pathol. 65, 101-106

Hanson,R.L., J.M.Benson, T.R.Henderson et al. (1985). Method for determining the lung burden of talc in rats and mice after inhalation exposure to talc aerosols. J. Appl. Toxicol. 5, 283-287

Hartge,P., R.Hoover, L.P.Lesher and L.McGowan (1983). Talc and ovarian cancer. J.A.M.A. 250, 1844

Karcioglu,Z.A., A.J.Aran, D.L.Holmes et al. (1988). Inflammation due to surgical glove powders in the rabbit eye. Arch. Opthalmol. 106, 808-811

Hildick-Smith,G.Y. (1976). The biology of talc. Br. J. Ind. Med. 33, 217-229

Hildick-Smith,G.Y. (1975). Talc - recent epidemiological studies. In: Inhaled particles IV, Walton, W.H. and B. McGovern (eds.) Pergamon Press, Oxford, pp 655-665

IARC (International Agency for Research on Cancer) (1987). Talc. IARC Monograph. Vol. 42, PP 185-224

ILO (International Labor Office) (1983). Encyclopaedia of occupational health and safety, 3rd ed., vol. 2, L. Permeggiani (ed.) Geneva.

Katsnelson,B.A. and K.A.Mokronosova (1979). Non-fibrous mineral dusts and malignant tumors. J. Occup. Med. 21, 15-20

Kleinfeld,M., J.Messite and M.H.Zaki (1974). Mortality experiences among talc workers: a follow-up study. J. Occup. Med. 16, 345-349

Kleinfeld,M., J.Messite and M.M.Langer (1973). A study of workers exposed to asbestiform minerals in commercial talc manufacture. Environ. Res. 6, 132-143

Kung, I.T.M., M.R.C.Path, F.B.Johnson et al. (1984). Blue bodies on cytology specimens in a case of pulmonary talcosis. Am. J. Clin. Pathol. 81, 675-678

Lamm,S.H., M.S.Levine, J.A.Starr and S.L.Tirey (1988). Analysis of excess lung cancer risk in short-term employees. Am. J. Epidemiol. 127, 1202-1209

Liebermann, J., A.Nosal, L.A.Schlessner and A.Sastre-Foken (1979). Serum-angiotensin-converting enzym for diagnosis and therapeutic evaluation of sarcoidosis. Am. Rev. Respir. Dis. 120, 329-325

Lockey,J.E. (1981). Nonasbestos fibrous minerals. Clinics in Chest Med. 2, 203-218

Lord,G.H. (1978). The biological effects of talc in the experimental animal: a litterature review. Fd. Cosmet. Toxicol. 16, 51-57

Moskowitz,R.L. (1970). Talc pneumoconiosis: a treated case. Chest 58, 37-41

Nam,K. and D.R.Gracey (1972). Pulmonary talcosis from cosmetic talcum powder. J.A.M.A. 221, 492-493

Natow,A.J. (1986). Talc: need we beware? Cutis 37, 328-329

Ng,T.K. (1984). Talc and mesothelioma. Med. J. Australia 140, 452-453

O'Connor,R.H., R.C.Brunham and D.H.Bowden (1988). Pulmonary talc granulomatosis mimicking pneumocystis carinii pneumonia. Canadian Med. Ass. J. 138, 53-54

Özesmi,M., T.E.Patiroglu, G.Hillerdal and C.Özesmi (1985). Peritoneal mesothelioma and malignant lymphoma in mice caused by fibrous zeolite. Br. J. Ind. Med. 42, 746-749

Parkes,W.R. (ed.). Talc pneumoconiosis. In: Occupational lung disorder. 2nd ed. Butterworth, London, 1982, pp. 296-310

Pelling,D. and J.G.Evans (1986). Long-term peritoneal tissue response in rats to mould-release agents and lubricant powder used on surgeon gloves. Fd. Cosmet. Toxicol. 24, 425-430

Von Püschel,K. und W.Schoof (1987). Zur Morphogenese hämatogen entstandener Fremdkörper-granulose in Lungenparenchym. Beitrage z. gerichtl. Med. 45, 121-128

Rohl,A.N. and A.M.Langer (1979). Fibrous mineral content of consumer talc-containing products. In: Dust and disease, Lemen, R., and J.M. Dement (eds.), Pathotox publishers Inc., Illinois, pp. 393-403

Rubino,G.F., G.Scansetti, G.Piolatto and C.A.Romano (1976). Mortality study of talc miners and millers. J. Occup. Med. 18, 186-193

Rubino,G.F., G.Scansetti, G.Piolatto and G.Gay (1979). Mortality and morbidity among talc miners and millers in Italy. In: Dust and disease, Lement, R. and J.M. Dement (eds.), Pathotox publishers Inc., Illinois, pp. 357-363

Selevan,S.G., J.Dement, J.K.Wagoner and J.R.Froines (1979). Mortality patterns among miners and millers of non-asbestiform talc: preliminary report. In: Dust and disease, Lemen, R. AND j.m. Dement (eds.), Pathotox publishers Inc., Illinois, pp 379-388

Stenbäck,F. and J. Rowland (1978). Role of talc and benzo(a)pyrene in repiratory tumor formation. An experimental study. Scand. J. Respir. Dis. 59, 130-140

Stille,W.T. and I.R.Tabershaw (1982). The mortality experience of upstate New York talc workers. J. Occup. Med. 24, 480-484

Thomas,T.L. and P.A.Stewart (1987). Mortality from lung cancer and repiratory disease among pottery workers exposed to silica and talc. Am. J. Epidemiol. 125, 25-43

Tuliainen,P., J.Nickels, E.Taskinen and M.Nyberg (1984). Br. J. Ind. Med. 41, 84-87

Vallyathan,N.V. and J.F.Craighead (1981). Pulmonary pathology in workers exposed to nonasbestiform talc. Humand Pathol. 12, 28-35

Wagner,J.C., G.Berry, R.J.Hill et al. (1979). An animal model for inhalation exposure to talc. In: Dust and disease, Lement, R. and J.M. Dement (eds.), Pathotox publishers Inc., Illinois, pp. 389-392

Wagner,J.C., G.Berry, T.J.Cooke et al. (1977). Animal experiments with talc. In: Inhaled particles IV, Walton, W.H. and B. McGovern (eds.), Pergamon Press, Oxford, pp. 647-652

Wegman,D.H., J.M.Peters, H.G.Boundy and T.J.Smith (1982). Evaluation of respiratory effects in miners and millers exposed to talc free of asbestos and silica. Br. J. Ind. Med. 39, 233-238

Wehner,A.P., B.D.Stuart and C.L.Sanders (1979). Inhalation studies with Syrian golden hamsters. Prog. Exp. Tumor Res. 24, 177-198

Wehner,A.P., G.M.Zwicker, W.C.Cannon et al. (1977A). Inhalation of talc baby powder by hamsters. Fd. Cosmet. Toxicol. 15, 121-129

Wehner,A.P., C.L.Wilkerson, W.C.Cannon et al. (1977B). Pulmonary deposition, translocation and clearance of inhaled neutron-activated talc in hamsters. Fd. Cosmet. Toxicol. 15, 213-224

Wehner,A.P., T.M.Tanner and R.L.Buschbom (1977C). Absorption and ingested talc by hamsters. Fd. Cosmet. Toxicol. 15, 453-455

Weissberg,D. (1984). Talc and adult respiratory distress syndrome (let. to ed.) J. Thorac. Cardiovasc. Surg. 87, 474-477

Wells,I.P., P.A.Dubbins and W.F.Whimster (1979). Pulmonary disease caused by the inhalation of cosmetic talcum powder. Br. J. Radiol. 52, 586-588

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Code		*Prijs*
RA 2/79	Koolmonoxyde	*f.* 23,=
RA 1/80	Fosfine	*f.* 12,=
RA 2/80	Anorganisch Lood	*f.* 18,=
RA 3/80	Carcinogene stoffen	*f.* 16,=
RA 4/80	Tolueen Diisocyanaat	*f.* 7,=
RA 5/80	Cadmium	*f.* 16,=
RA 6/80	Chloor	*f.* 13,=
RA 1/81	n-Heptaan	*f.* 11,=
RA 2/81	Pentaan	*f.* 9,=
RA 3/81	1,1,1-Trichloorethaan	*f.* 18,=
RA 4/81	Formaldehyde	*f.* 17,=
RA 5/81	Metallisch Kwik	*f.* 13,=
RA 1/82	Mangaan	*f.* 17,=
RA 2/82	Monochloorethaan	*f.* 11,=
RA 3/82	Anorganische Kwikzouten	*f.* 15,=
RA 4/82	Organische Kwikverbindingen *(Uitsluitend phenylkwik en alkoxyalkylverb.)*	*f.* 13,=
RA 5/82	Kwikalkylverbindingen - Korte keten *(Uitsluitend methylkwik en ethylkwik)*	*f.* 18,=
RA 1/83	Methyleenchloride	*f.* 17,=
RA 2/83	Triethylamine	*f.* 16,=
RA 3/83	Trichloorethyleen	*f.* 18,=
RA 1/84	Asbest	*f.* 28,=
RA 2/84	Anorganische Arseenverbindingen *(Exclusief Arseenwaterstof)*	*f.* 20,=
RA 4/84	Caprolactam	*f.* 17,=

Code		Prijs
RA 1/85	2-Nitropropaan	*f*. 12,=
RA 2/85	Lachgas	*f*. 21,=
RA 3/85	Nikkel en nikkelverbindingen	*f*. 21,=
RA 4/85	Zwaveloxide	*f*. 17,=
RA 5/85	Stikstofoxide	*f*. 15,=
RA 6/85	Chroom en chroomverbindingen	*f*. 20,=
RA 1/86	Epichloorhydrine	*f*. 19,=
RA 1/87	1,4-Dioxaan	*f*. 13,=
RA 2/87	Hydrazine, dimethylhydrazine, hydroxyethylhydrazine en fenylhydrazine	*f*. 21,=
RA 3/87	Formaldehyde *(Engelse uitgave)*	*f*. 22,=
RA 4/87	4,6-Dinitro-ortho-cresol	*f*. 13,=
RA 5/87	Dibroomethaan	*f*. 13,=
RA 6/87	Aflatoxine B1, B2, G1 en G2	*f*. 16,=
RA 7/87	Chloroform	*f*. 18,=
RA 8/87	1,1-Dichloorethaan	*f*. 9,=
RA 9/87	Trimethylamine	*f*. 13,=
RA 10/87	Vanadium metaal en anorganische verbindingen	*f*. 16,=
RA 11/87	n-Hexaan	*f*. 21,=
RA 12/87	2-Propoxyethanol, 2-Propoxyethylacetate, 2-Isopropoxyethanol *(Engelse uitgave)*	*f*. 9,=
RA 13/87	Acrilaten	*f*. 13,=
RA 14/87	Trichlorofluoromethane *(Engelse uitgave)*	*f*. 16,=
RA 15/87	Fluorcarbons(except FC11) *(Engelse uitgave)*	*f*. 21,=
RA 1/88	Para-Dichloorbenzeen	*f*. 15,=
*** RA 2/88	Hexachlorobenzene	*f*. 24,=
RA 3/88	Carbonylfluoride and PTFE Pyrolysis products	*f*. 11,=

Code		*Prijs*
RA 4/88	Beryllium and Beryllium compounds	*f*. 22,=
RA 1/89	Fluorine, Hydrogenfluorine and Inorganic fluorine compounds	*f*. 22,=
RA 2/89	Aniline	*f*. 17,=
RA 3/89	Phtalic anhydride	*f*. 12,=
RA 4/89	Ethyl Methanesulphonate (EMS) Methyl Methanesulphonate (MMS)	*f*. 22,=
RA 5/89	Benzeen *	*f*. 10,=
RA 6/89	Ethyleenoxide *	*f*. 13,=
RA 7/89	Selenium en verbindingen *	*f*. 18,=
RA 8/89	Styreen *	*f*. 17,=
RA 9/89	Evaluatie van risico op kanker bij beroepshalve blootstelling aan asbest (aanvullend op RA 1/84) *	*f*. 12,=
RA 1/90	Methyl acrylate	*f*. 14,=
RA 2/90	2-Hexanone	*f*. 17,=
RA 3/90	Cyclohexanol	*f*. 16,=
RA 4/90	Amyl acetate	*f*. 11,=
RA 5/90	1,3-Butadiene	*f*. 17,=
RA 6/90	Ethyl acrylate	*f*. 15,=
RA 7/90	Ethyl amine	*f*. 13,-
RA 8/90	Gezondheidskundige aspecten van het begrip Blootstelling en van het meten/schatten ervan *	*f*. 26,-
RA 9/90	Fijn hinderlijk stof; gezondheidskundige aspecten van bijlage 3 bij de Nationale MAC-lijst 1989 *	*f*. 22,-
RA 10/90	Dimethylamine	*f*. 16,-
RA 11/90	Thiourea	*f*. 11,-
RA 12/90	Dimethyl- en diethylsulfaat *	*f*. 14,-

Code		Prijs
RA 13/90	Methylbromide	f. 18,-
RA 14/90	7/8 Carbon chain Aliphatic Monoketones	f. 17,-
RA 15/90	Cyclohexane	f. 14,-
RA 16/90	Methyl ethyl ketone	f. 17,-
RA 1/91	Tetrahydrofuran	f. 18,-
RA 2/91	Tolueen *	f. 21,-
RA 3/91	Diisocyanates	f. 22,-
RA 4/91	Methyl isobutyl ketone	f.
RA 5/91	Xylene	f.

*** Alle rapporten vanaf RA 2/88 zijn Engelstalige uitgaven voorzien van een Nederlandstalige samenvatting uitgezonderd de rapporten voorzien van *