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INTEGRATED CRITERIA DOCUMENT ASBESTOS

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CONTENTS

SUMMARY

This document contains data on asbestos concerning the sources and distribution pattern (soil, water, air), the risks to man in particular at current exposure levels, and the technical possibilities and economic consequences of reducing these risks. This information provides the scientific basis for the formulation of the effect-directed standardization policy. Since the risks remain confined to exposure via the respiratory route, the emphasis is especially on the environmental compartment air.

Asbestos is the generic name used for a family of fine anorganic fibres (mineral silicates), which can be classified either as serpentine (chrysotile) or amphibole (the other commercial asbestos types). Because of its thermal stability and chemical resistance, its electrical insulating property and high tensile strength, asbestos had a wide range of applications in the past. As a result of the now-known drawbacks of asbestos and the consequent regulations, the number of uses and total consumption in the Netherlands have fallen sharply in recent years.

Chrysotile is the only asbestos variety still processed in the Netherlands. The form in which asbestos is released differs from one environmental compartment to another.
Emission into the soil occurs chiefly from the dumping of waste products; soil contamination as a result of deposition and infiltration is relatively small. It concerns an annual total of about 4500 tonnes (in 1982), divided between bound (52%) and unbound (13%) asbestos and asbestos as a fraction of a very large waste stream (35%).
The emission into surface water was over 2.7 tonnes in 1982. This has meanwhile been cut back to 1.4 tonnes.
In 1982, about 2,3 tonnes were emitted into the air in the Netherlands, consisting for the most part of free asbestos fibres. In addition to a number of localized sources, there are significant diffuse sources. The principal emissions are caused by brake dust on roads (26%), processing of asbestos cement on site (20%), the manufacture of braking and friction materials (13%), the demolition of buildings and rubble breaking (12%), and brake dust in garages (16%). It is expected that these emissions will have risen by about 50% by the year 2000. The reasons for this are (a) the presence of more asbestos in buildings that are due for renovation or demolition in the coming decades, and (b) the growth in road traffic.

Chrysotile is the principal asbestos type involved in these emissions; other asbestos varieties can only be of local importance. Re-emissions of fibres can contribute significantly to the asbestos load in the air; asbestos fibres are relatively inert and can consequently circulate in the environment for long periods of time. However, the extent of the contribution of re-emissions cannot be estimated at present.

Asbestos is the subject of much attention especially because of its effects on the health of man. The principal effect is the development of bronchial carcinomas (lung cancer) and mesotheliomas (tumours of the pleura and peritoneum) following exposure via the respiratory route. There is no evidence of a carcinogenic effect following exposure via the gastrointestinal tract. It is assumed that the current exposure level via the oral route involves a negligible risk.
The carcinogenic activity of asbestos at exposure via the respiratory route depends on the shape of the fibres (length/diameter ratio of at least 3), and especially on their dimensions. The critical fraction encompasses all respirable chrysotile and amphibole fibres with a length of more than 5 μm and a diameter of less than 3 μm, the most dangerous being fibres with a diameter of around 0.1-0.2 μm. As regards the development of mesotheliomas, the durability of the fibres in the body is also relevant. In this connection, chrysotile, which dissolves slowly in the lung tissue, seems to be less hazardous than the amphiboles.
The optical microscope measuring methodology, which is in routine use, is not satisfactory for the detection of fibres with the above-mentioned dimensions. For this electron microscope analysis techniques must be used. There is an urgent need here for a standardized method of assessing environmental samples.

In view of the carcinogenic properties of asbestos after inhalation, exposure via the respiratory route should be avoided as far as possible. There are no quality requirements for the outdoor air in the Netherlands. To make a risk estimate for the purpose of possible future standards for the environment, the WHO guideline was used, with a modification regarding chrysotile asbestos. The WHO guideline is based on extrapolation of data from occupationally exposed individuals to the general population with an estimated 30% smokers (smoking increases the risk of lung cancer from exposure to asbestos). The estimated approximate risks to the general population at lifetime exposure to asbestos, measured as described above,

indicate that exposure to chrysotile is associated with an excess of lung cancer, whereas the amphiboles cause an increased risk of developing mesotheliomas.

A lifetime risk of 10^{-6} (one excess death from mesotheliomas or cancer of the lung per 1000,000 total deaths) will be caused by lifelong exposure to an estimated 10 to 100 amphibole fibres per m^3 (mesotheliomas), and by lifelong exposure to an estimated 100 to 1000 chrysotile fibres per m^3 (lung cancer in a population with 30% smokers).

Comparison of the exposure levels in the ambient air with this toxicological risk estimate shows that the expected lifetime risk of lung cancer in the immediate vicinity of asbestos sources and in a number of large cities and industrial areas is higher than 10^{-6}. In one area where amphibole asbestos was detected in the ambient air, the expected lifetime risk of mesotheliomas is also higher than 10^{-6}. The expected risks across the Netherlands remain below 10^{-4} (10^{-6} per year), which the IMP-Environmental Management 1986-1990 considers to be the maximum allowable risk*. It is not known to what extent this maximum allowable risk is exceeded in the immediate vicinity of the numerous diffuse sources (garages, waste disposal sites, and the like).

Risk groups which may be exposed to high asbestos levels are (in addition to the workers in the asbestos-manufacturing and -processing industries) persons who, by virtue of their profession, spend long periods of time in public buildings and offices where sprayed asbestos has been applied, and demolition workers. Heavy physical exertion increases the respiration rate and thereby the exposure dose. Smokers constitute a risk group with an increased susceptibility to lung cancer.

*) The effect-directed standardization policy, as laid down in the IMP-Environmental Management 1986-1990, considers a lifetime risk of 10^{-6}, corresponding to 1 in 10^8 cases per year, to be the so-called negligibility level. This policy considers a lifetime risk of 10^{-4}, corresponding to 1 in 10^6 cases per year, to be the maximum allowable risk. This risk is caused by lifelong exposure to an estimated 1,000-10,000 amphibole fibres per m^3 (mesotheliomas), and an estimated 10,000-100,000 chrysotile fibres per m^3 (lung cancer in a population with 30% smokers).

In the case of an autonomous development, the emission into the air will increase in the near future. This increase is expected as a consequence of the presence of more asbestos in buildings that are due for renovation or demolition (a factor of 3 higher by the year 2000) and the growth in road traffic (50% higher emission by 2000 due to an increase in brake dust). There is the possibility that, if measures are not taken, the limits of the maximum allowable lifetime risks established by the standardization policy will be exceeded within a few decades. Measures aimed at controlling the emission of asbestos during all stages of the life cycle of asbestos-containing materials are therefore advisable. As regards the emissions during demolition and renovation activities, these can be reduced by about 90% at an annual cost of f 5500 (f 30 per kg asbestos emission avoided). To reduce asbestos emissions from braking and friction materials, it seems desirable that the use of substitutes be encouraged. However, it should be borne in mind that alternative materials may have a similar biological effect to asbestos. This should be evaluated for each material and application area.

INTRODUCTION

Environmental policy at government level is first of all aimed at attaining and maintaining an air quality which ensures the general health and wellbeing of man and the preservation of animals, plants, goods, as well as specific uses of the substance in question (Indicative Multi-year Programme - Environmental Management 1986-1990). However, with insufficient knowledge it is impossible for the time being to describe fully the overall environmental quality in view. Attention is therefore being concentrated on factors which probably entail considerable risks, including environmentally harmful substances. A selection has been made of the many substances of relevance, because of emission or use, and a priority list compiled. In principle, so-called integrated criteria documents are drawn up for most of the priority substances.
Integrated criteria documents contain, per substance or substance group, data on the sources and the distribution pattern (soil, water, air, biota), the risks of actual exposure concentrations for man, (parts of) ecosystems and materials, and the technical and economic possibilities of reducing these risks. This information serves as the scientific basis for formulating the effect-directed environmental policy. This may lead to environmental quality requirements and a general task-setting for the emission reductions per source.

This document deals with asbestos. Asbestos is the generic name used for a group of fine anorganic fibres (mineral silicates); on the basis of the number of fibrous varieties of the minerals, different types of asbestos are encountered. Asbestos has been known for more than 4000 years and is widely used, especially because of its resistance to fire and its great tensile strength. The hazard to public health was recognized about 60 years ago. Up till about 1970, a fair amount of research had been carried out into the principal effects: the development of asbestosis (a disease of the lung caused by exposure to asbestos dust), carcinoma of the lung and mesothelioma (a form of cancer on the visceral pleura). In the subsequent period many evaluation reports were published, which helped to establish the current standards. In point of fact, this means that these standards are based on the relatively inadequate knowledge about the dose-response relationships in the work environment of at least 15 years ago, using an optical microscope as the measuring instrument. This microscope can only

detect fibres with a diameter of more than 0.3 μm. These fibres are not very common in the outdoor air. Newer measuring techniques are now available for thinner fibres. In addition, in view of the difference in shape and dimensions of fibres in the workplace and in the ambient air, a fundamentally different risk evaluation may be advisable. The emphasis in the present document is therefore on gaining an insight into how useful the available data are for determining the (potential) risks to the general population.

This document was prepared by the National Institute of Public Health and Environmental Protection (RIVM) in collaboration with third parties, namely: the Netherlands Organization for Applied Scientific Research (TNO), DHV Consulting Engineers BV, the Institute for Environmental Issues (IvM), and the Economic and Social Institute of the Free University of Amsterdam (ESI).

For some sections, valuable information was obtained from relevant industrial sectors; their cooperation was procured through the Office of Environment and Physical Planning of the Council of Dutch Employers' Unions. The document has been checked in its entirety by a Reviewing Committee of the RIVM and submitted to interest groups and advisory bodies for comments. A Supervisory Group comprising staff from the Ministry of Housing, Physical Planning and the Environment, the Department of Inland Waterways/National Institute for Waste Water Purification (RIZA) and the Ministry of Agriculture and Fisheries also gave guidance in the preparation of this doument.

1. PROPERTIES OF ASBESTOS AND EXISTING STANDARDS

1.1. MATERIAL PROPERTIES

1.1.1. Structure and theoretical formula

Asbestos is the generic name used for a number of naturally occurring anorganic silicates. Two main groups can be distinguished: the serpentine and the amphibole groups. The six technically most important minerals are classified as given in figure 1.1. (Zielhuis, 1977).

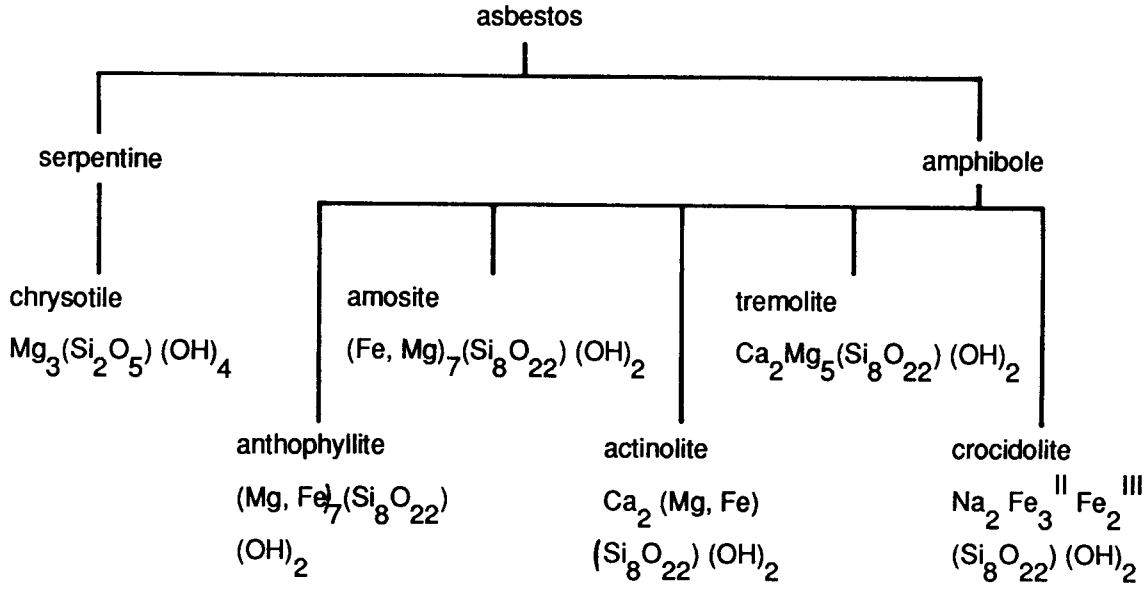

Figure 1.1. Asbestos types and chemical composition

A relatively large variation in fibre structure is possible within each asbestos type, which is probably caused by small variations in the crystalline structure. As a result of these variations, there are differences in physical and chemical properties. The chemical composition and the crystal structure of asbestos are also of vital importance for its technical application. Fibres with a high magnesium content look silky white and may be less than 0.3 μm in diameter. On the other hand, fibres with a high iron content have a straight, brittle texture and the diameter is at least 0.1 μm.

Chrysotile, which contains much magnesium, can be defined as a sheet silicate, with the flat structure rolled about an axis, forming a narrow tube, called a fibril, thereby endowing it with strength and flexibility. Chrysotile is "curly". A macro-fibre consists of a large number of fibrils. The structure of amphiboles is formed by a double chain of silica tetrahedra, separated by a cation chain. The most common cations are Mg^{2+}, Fe^{2+}, Fe^{3+}, Na^{+} and Ca^{2+}. Cation substitution by small amounts of Al^{3+}, Ti^{4+}, K^{+} and Li^{+} is possible. Because of this rigid structure, these fibres are coarser and more brittle.

1.1.2. Registration numbers

Table 1.1. CAS and RTECS numbers of the different asbestos types (NIOSH, 1983)

Asbestos type	*CAS*	*RTECS*
Asbestos	*1332 - 21 - 4*	*CL 6475000*
Chrysotile	*12007 - 29 - 5*	*GC 2625000*
Anthophyllite	*17068 - 78 - 9*	*CA 8400000*
Amosite	*12172 - 73 - 5*	*BT 6825000*
Actinolite	*12172 - 67 - 7*	*AU 0550000*
Tremolite	*14567 - 73 - 8*	*XX 2095000*
Crocidolite	*12001 - 28 - 4*	*GP 8225000*

1.1.3. Nomenclature and synonyms

Table 1.2. Mineral names of the principal asbestos types (NIOSH, 1983)

Mineral name	*the Netherlands*	*Britain*	*West Germany*
	asbest	*asbestos*	*Asbest*
Serpentine	*chrysotiel*	*chrysotile*	*Chrysotil*
Anthophyllite	*anthofylliet*	*anthophyllite*	*Anthophyllit*
Grunerite	*amosiet*	*amosite*	*Amosit*
Actinolite	*actinoliet*	*actinolite*	*Actinolit*
Tremolite	*tremoliet*	*tremolite*	*Tremolit*
Riebeckite	*crocidoliet*	*crocidolite*	*Krokydolit*

Chrysotile, amosite and crocidolite are also known as white, brown and blue asbestos respectively.

1.1.4. Physical and chemical properties

The best known property of all types of asbestos fibre is their resistance to heat. The asbestos varieties are degraded to simple structures by dehydroxylation and dehydrogenation upon heating to a temperature of between 400 and 1000 ^{o}C.

Chrysotile is rapidly degraded by strong acids, whereas amphibole fibres are to some degree resistant to acids. Strong alkalis have very little influence on all asbestos fibres, especially chrysotile, making this fibre particularly suitable for the reinforcement of cement.
The most important physical properties of asbestos fibres are their high tensile strength and stiffness, making them extremely suitable for composite structures. Fibre/polymer strength ratios of the order of 100 to 1 and stiffness ratios of between 20 and 40 to 1 are possible.
The length of the asbestos fibres varies enormously and is dependent on the type of asbestos, the originating mine and the extent and method of treatment. Asbestos fibres can be split into smaller fibres. Industry exploits this property by treating raw asbestos chemically or mechanically. The degree of "fibrilization" determines the specific surface area and thereby the industrial application (table 1.3.). Raw asbestos has a specific surface area of 6,000-30,000 $cm^2.g^{-1}$, which can increase by a factor of 5-6 through industrial processing.

Table 1.3. Average fibre length and diameter with different applications

	Textiles	*Insulation boards*	*Asbestos cement*	*Braking material, paper, millboard*	*Plastics, fillers, floor tiles*
Fibre length (mm)	*8-24*	*5-17*	*2-13*	*2-4*	*1-3*
Fibre diameter (µm)	*0.03-100*	*0.03-100*	*0.03-100*	*0.03-100*	*0.03-100*

Conversion factors

In the Dutch situation, 1 ng in the outdoor air corresponds to 2,000 to 40,000 fibres. Depending on the type and age of the fibre and its source, the ratio between the number of fibres as determined by electron microscopy (EM) and light microscopy (LM) can vary considerably. For example, Cherrie et al. (1987) found an EM/LM ratio of 0.05 to 13 for fibres with a length of > 5 µm for the ambient air. Because of such findings it is not possible to give a generally applicable conversion factor; it will differ from one location to another.

The characteristics, composition and properties of the six principal asbestos types are presented in table 1.4.

Table 1.4. Characteristics of the principal types of asbestos fibre

	Chrys.	Crocid.	Amosite	Anthoph.	Tremolite	Actinolite
Content (%)						
SiO_2	38-42	49-56	49-52	53-60	55-60	51-56
Al_2O_3	(0-2)*	(0-1)	(0-1)	(0-3)	(0-3)	(0-3)
Fe_2O_3	(0-5)	13-18	(0-5)	(0-5)	(0-5)	(0-5)
FeO	(0-3)	3-21	35-40	3-20	(0-5)	5-15
MgO	38-42	(0-13)	5-7	17-31	20-25	12-20
CaO	(0-2)	(0-2)	(0-2)	(0-3)	10-15	10-13
Na_2O	(0-1)	4-8	(0-1)	(0-1)	(0-2)	(0-2)
H_2O	11.5-13	1.7-2.8	1.8-2.4	1.5-3.0	1.5-2.5	1.8-2.3
Colour	usually white to pale green; yellow, pink	blue	pale grey to light brown	white to grey; light brown	white to grey	pale to dark green
decomposition temp. (^{o}C)	450-700	400-600	600-800	600-850	950-1040	620-960
melting temp. of residual material (^{o}C)	1500	1200	1400	1450	1315	1400
Density ($kg.m^{-1}$)	2550	3300-3400	3400-3500	2850-3100	2900-3100	3000-3200
Resistance to acids	poor	good	moderate	very good	very good	moderate
Resistance to alkali	very good	good	good	very good	good	good
Tensile strength ($N.m^{-2}$)	30	34	17	(<7)	5	5
Texture	usual flexible, soft, smooth and ductile	flexible to brittle and ductile	usual brittle	usual brittle	usual brittle	

* (often present)

1.2. STANDARDS AND RECOMMENDED VALUES

1.2.1. Soil

There are no asbestos standards for soil.

1.2.2. Water

A directive has been drawn up within the EEC (1987) which prescribes that waste water from the asbestos-processing industry should be completely recycled. If recycling in the manufacture of asbestos cement is economically not feasible, then a limit of 30 g of total suspended particles per m^3 of waste water is applicable. This limit also applies to cleaning operations and repair work on the installations at companies producing asbestos paper and millboard. The permitted volume of waste water may be determined by the member states.

1.2.3. Air

In the workplace

In the Netherlands, the regulations of the Asbestos Decree are in force for working with asbestos.

The MAC value for asbestos (except crocidolite) is 2 fibres per ml of air, as determined by phase contrast optical microscopy. An asbestos fibre is defined as a particle with a length of > 5 μm and a length/diameter ratio of at least 3 : 1 (ARBO, 1977). For work on crocidolite-containing asbestos cement pipes, an exemption can be granted from the ban, included in this Decree, on processing crocidolite or crocidolite-containing materials or products (ARBO, 1984). To this exemption, the regulation is attached that the concentration of crocidolite dust in the inhaled air may not exceed a value of 0.2 fibres per ml of air, as determined by phase contrast optical microscopy and measured over a reference period of 10 minutes.

According to the National MAC list (1986), exposure to asbestos (except crocidolite) may not exceed 2 fibres per ml of air as a time-weighted average over a period of 4 hours, with a limit of 12 fibres per ml of air measured over any 10-minute period being the maximum permitted. The MAC value is currently under consideration. To this end, the Working Party of experts of the Labour Directorate-General has published an evaluation

report (WGD, 1984). Table 1.5. lists the MAC values for a few leading countries.

Table 1.5. Air quality in the workplace (MAC values, time-weighted averages) for a few countries, in number of fibres per cm^3

Country	Fibre type	MAC value	Measurement period (hr)	Remarks	Reference
EEC	crocidolite	0.5	8		EG (1983)
	other types	1	8		
	mixture**	0.5-1	8	**	
US	asbestos	2	8	length >5 μm	
		10	0.25		
		0.1*	8		
		0.5*	0.25		
	amosite	0.5	8	TLV	ACGIH (1985)
	chrysotile	2*	8		
	crocidolite	0.2*	8		
	other types	2*	8		
West Germany	asbestos	1	8	TRK	KPADF (1987)
	asbestos-containing fine dust	2.0($mg.m^{-3}$)	8	1>5 μm; d<3 μm 1: d≥ 3:1	
Britain	chrysotile, amosite and fibrous antho-phyllite	2.0	4	1>5 μm 1: d≥ 3:1	Zielhuis (1977)
		12	0.25		
	crocidolite	0.2	0.25		
	crocidolite	0.2*	4		HMSO(1979)
	chrysotile	1*	4		
	amosite	0.5	4		

* recommendations

** MAC value in the ratio of the composition of crocidolite/other types in the mixture

Ambient air

Table 1.6. gives a few standards for the asbestos concentration in the outdoor air.

Table 1.6. Environmental quality requirements for the outdoor air, in $mg.m^{-3}$

Country	Standard	Details	Reference
US (proposal)	0.00003	monthly average	Bruckman and Rubino (1975)
USSR	0.15	daily average	Zielhuis (1977)
	0.5	max. concentration in dust sample	

During both the production of raw asbestos, and the use of asbestos in the industrial finishing of a number of products, the concentration of the asbestos emitted into the air via ducts may not exceed the limit of 0.1 mg per m^3 of waste gas. For installations producing less than 5000 m^3 of waste

gas per hour, the emission of asbestos should never exceed 0.5 g asbestos per hour under normal operating conditions (EG, 1987).

1.2.4. Products and waste materials

Asbestos-bearing articles, except semifinished products, may only contain asbestos fibres which are each tightly and durably bound to the matrix. Asbestos-containing articles are considered to be tightly bound when they have a quality factor of 0.35 or more as determined by a specified testing method. These articles should be provided with one or more indications showing clearly the presence of asbestos and the precautionary measures to be taken (Warenwet (Commodities Act), 1983).

Toys may not consist of asbestos, either wholly or partially (Warenwet, 1985). It is prohibited to spray asbestos or asbestos-containing materials or products (ARBO, 1977). The Chemical Waste Act (WCA, 1977) regards waste as chemical waste when the asbestos concentration is higher than 25 $g.kg^{-1}$.

An EEC directive (1985) specifies products which are not permitted to be marketed or used. They include, among other things, toys, paint, varnish, and materials or preparations designed to be applied by spouting or spraying.

Asbestos has been included in the EEC's list of toxic and hazardous waste materials, for which a directive is in force as regards collection, separation, transport and treatment (EG, 1978).

Talc, which is permitted as an anti-hygroscopic agent, can sometimes contain actinolite as a natural contaminant. The use of talc is restricted (Staarink and Hakkenbrak, 1982; 1985).

2. PRODUCTION, APPLICATIONS, SOURCES AND EMISSIONS

2.1. PRODUCTION AND APPLICATIONS

2.1.1. Production

World production of raw asbestos amounted to nearly 5 million tonnes in 1979 and 1980, and has been almost 4 million tonnes since 1982. The major producing countries are the USSR (about 50% of world production), Canada (about 20%) and the Republic of South Africa (about 5%). The stable production since 1982 and thereby thus also the constant consumption is to a considerable extent due to the growing consumption in the industrializing countries. In Europe, the US and Japan, the use of asbestos is declining. Total consumption in the Netherlands is only a small fraction of this. In 1982, over 5 ktonnes was imported as raw asbestos. The net import of asbestos (including asbestos in products and minus the re-exported asbestos in products) was 15.6 ktonnes.

2.1.2. Applications

Because of its resistance to heat, chemical and electrical effects, and its high tensile strength, asbestos fibre has a multitude of uses. It has been and is specifically used as a reinforcing agent in such products as asbestos cement, brake linings, floor coverings, mastics, concrete adhesives, paints, roofing bitumen, etc. It is ideal for materials designed to protect against heat in fire-proofing (e.g. sprayed insulation) and in heat-resistant clothing. The number of applications has fallen drastically because of the currently known drawbacks of asbestos and the consequent regulations. Total consumption has also decreased. Asbestos is now only used in a limited number of products. The use of crocidolite has been prohibited in the Netherlands since 1977, both in pure form and in products. Furthermore, the spraying of asbestos is forbidden, as a result of which amosite is also no longer used. For application of asbestos-cement pipes containing crocidolite, an exemption was granted until the end of 1985, in order to use up existing stocks. The situation in 1986 was that the greater part of the asbestos still used found application in the construction industry, chiefly in asbestos-cement sheets for roofs, exterior wall elements, lining of inner cavity walls, and the like, and in

drinking-water and waste-water (pressure) pipes. Another important remaining use is in braking and friction materials (mostly in brakes for vehicles). Of relatively minor importance is its application in sealing materials for the petrochemical industry. Application as insulation in electrical appliances and as reinforcement in auxiliary materials used for construction, such as mastics, adhesives and coatings has all but ceased. Until about 1978, all above-mentioned products were also produced in the Netherlands or imported. As a result of the Asbestos Decree, the processing of raw asbestos in the Netherlands has fallen sharply. The decrease in production is probably caused by the economic recession, while for other products the reduction is the result of changing to products without asbestos. The production of asbestos fibre-reinforced floor coverings and the manufacture of asbestos paper, millboard and products for insulation and sealing containing asbestos was discontinued after 1982. The production of asbestos-cement pipes has been transferred to other countries. Since 1978, sprayed insulation is no longer applied. The decreased usage of raw asbestos and asbestos-containing products and in particular the cessation of the production of asbestos fibre-reinforced floor coverings are most clearly reflected in the import figures (table 2.1.).

Table 2.1. Net import figures for 1976-1985, in ktonnes per year (CBS, 1986)

Year	*Raw asbestos*	*Amount of asbestos in asbestos cement*	*Amount of asbestos in other products*	*Net total import of asbestos*
1976	*49.4*	*15.3*	*-20.3**	*44.4*
1977	*39.0*	*14.9*	*-17.0**	*36.9*
1978	*41.4*	*14.5*	*-16.5**	*39.3*
1979	*28.2*	*16.1*	*- 9.9**	*34.4*
1980	*18.7*	*19.0*	*- 7.1**	*30.5*
1981	*9.7*	*9.4*	*- 0.8**	*18.3*
1982	*5.0*	*9.8*	*0.8*	*15.6*
1983	*5.5*	*11.5*	*0.5*	*17.5*
1984	*8.1*	*11.1*	*1.0*	*20.2*
1985	*5.6*	*9.6*	*1.3*	*16.5*

** export, chiefly of asbestos paper, felt and millboard with rubber, incorporated into, among other things, floor coverings*

It is clear that in terms of percentage the import of raw asbestos has decreased much more sharply than the net total import. There has been a large relative shift from domestic production to imports in response to the above-mentioned statutory measures. The number of companies importing

and/or processing asbestos, or supplying asbestos-containing products on a large scale, has also fallen.

Table 2.2. gives a summary of the processing and application of asbestos-containing materials in the Netherlands in 1982. It shows that the asbestos-cement products constitute the most important product group as regards both total product volume and asbestos fibre usage.

Tables 2.3. and 2.4. give a breakdown for the two principal product groups asbestos cement and braking materials.

Table 2.2. Production and domestic sales of asbestos-containing products in 1982, in ktonnes per year (DHV, 1984)

Category	Production in the Netherlands	Net import	Total consumption in the Netherlands	Proportion of total asbestos consumption
	Product/ Asbestos	Product/ Asbestos	Product/ Asbestos	%
- Asbestos cement products	47.5 / 4.5	71.4 / 8.9	118.9 / 13.4	82.7
- Braking and friction materials	2.6 / 0.97	0.36/ 0.16	2.9 / 1.05	6.4
- Insulating, packing, sealing material (fabric, paper, millboard, felt with or without rubber)	0.73/ 0.66*	0.34/ 0.24	1.07/0.9	5.4
- Bitumen products, mastics, adhesives, coatings	13.4 / 0.40	2.7 / 0.31**	16.1 / 0.71	4.3
- Floor covering (rolls and tiles)	- / -	1.05/0.17****	1.05/ 0.17	1.0
- Electrolysis diaphragms	0.03/ 0.03	- / -	0.03/ 0.03	0.2
- Liquid filters	- / -	0.002/0.0004	0.002/0.0004	-
Total	6.50***	9.78	16.26	100

* production ceased in the Netherlands as from 1982
** estimated
*** deviates from the net import estimate given in table 2.1. because of the stock of asbestos fibres being used up by the primary processors
**** 0.4 ktonnes per year is domestic production based on imported asbestos felt with rubber

Table 2.3. Consumption of asbestos cement products in the Netherlands in 1982 (DHV, 1984)

Product	*Consumption (ktonnes/yr)*	*Proportion of total consumption (%)*	*Area of application*
- Corrugated sheets	*59.3*	*50*	*outdoors*
- Slates	*0.3*	*< 1*	*outdoors*
- Sheets	*28.0*	*24*	*60-65% indoors (e.g. inner cavity wall) 35-40% outdoors (e.g. exterior wall cladding)*
- Pipes	*24.2*	*20*	*30-35% sewerage 65-70% drinking water*
- Others	*7.1*	*6*	*cisterns, ventilation ducts*
Total	*118.9*	*100*	

Table 2.4. Production and net import of brake linings, brake pads and friction materials in 1982 (DHV, 1984)

Product	*Production (kt/yr)*	*Net import (kt/yr)*	*Proportion of asbestos (%)*	*Asbestos accumulation (kt/yr)*
- Disk brake pads	*1.6*	*-0.48*	*35*	*0.39*
- Brake linings and clutch facings	*1.0*	*0.70*	*35*	*0.6*
- Industrial friction material	*-*	*0.15*	*55*	*0.08*
Total	*2.6*	*0.37*		*1.07*

2.1.3. Consumption and accumulation

On the basis of known import-export statistics (CBS, 1986), it can be calculated that 1250 ktonnes of asbestos have been used in the Netherlands for domestic consumption since 1920. Estimates (De Vos, 1981) show that about 575 ktonnes of asbestos are present in buildings. About 175 ktonnes are present in pipes and several ktonnes in the other applications (with a relatively short useful life) (table 2.5.).

This means that about 500 ktonnes of asbestos have already been dumped as waste, for the most part building and demolition waste. In addition, a not inconsiderable amount of waste will have been generated directly in the production and processing of raw asbestos, viz. 5-10% of the total roughly 1250 ktonnes processed. This percentage is likely to have been 10% or more in the past.

Table 2.6. summarizes the accumulation of asbestos.

Table 2.5. Asbestos-containing materials present in buildings (De Vos, 1981) and pipes for waste-water pressure pipe systems and drinking-water distribution networks (KIWA, 1986)

Product	Amount (ktonnes)	Portion of asbestos (ktonnes)
Present in buildings:		
- asbestos-cement corrugated sheets	2,544	254
- asbestos-cement flat sheets	1,504	203
- other asbestos-cement products	561	98
- vinyl-asbest floor covering (ca. 1 mln m^2)	3	1
- foam-backed vinyl, and asbestos paper (7-10 mln m^2)	21	1
- insulation products, incl. sprayed layers	ca. 5	4
- fillers and reinforcement*	ca. 300	15
Present in pipe systems:		
- drinking-water pipes	890**	156
- waste-water pressure pipes	62.5***	11
Total		743

* assuming that a small part is felt, millboard and paper with a high asbestos content (90%) and the greater part is roof bitumen, mastics, adhesives, paints and the like with an average low asbestos content (3%)

** as from 1983 (KIWA, 1986)

*** estimated

Table 2.6. Total amount of asbestos present in the Netherlands in 1982, in ktonnes

Total domestic consumption since 1920:	1,250
Present in:	
- buildings	576
- asbestos-cement pipes	167
- other products	ca. 5
	750
Already dumped as :	
- production and processing waste	125
- construction and demolition waste	265
- other waste*	110
	500

* on the basis of a division into 90% applications in asbestos cement and 10% in other products with a relatively short useful life

Of the asbestos still present in durable applications, about 20 ktonnes are crocidolite (chiefly in asbestos-cement pressure pipes) and about 4 ktonnes are amosite (mainly in sprayed insulation).

2.2. SOURCES AND EMISSIONS

2.2.1. Natural sources

Asbestos-bearing rock is quite common in Europe. There is a large open-pit mine at Balangero (Italy) (Lanting and Den Boeft, 1979). However, asbestos-bearing rock does not occur in the Netherlands (Den Boeft and Lanting, 1981). Since asbestos fibres can be transported over considerable distances via both air and water, it is probable that in the Netherlands natural sources make a very small contribution to concentration levels in air and water. Quantification of its extent is almost impossible.

2.2.2. Primary emissions

Emissions of asbestos into soil, water and air occur during all stages in the life of an asbestos-containing product. These products differ widely one from another as to how the asbestos has been incorporated into them, in the manner it is bound in them and in the type of application. It is therefore useful to look at the emissions per product during the successive phases of use.
The emission factors in the following paragraphs have been estimated from literature data or, if not available, on the basis of comparison, taking into account the degree of bonding of the asbestos and, where known, the particle concentration in the immediate vicinity of such a source. Another basis for emission factors is the useful life of a product and the anticipated wear. Both are dependent to a large extent on the application of the product and the circumstances under which it is used. Estimates therefore provide no more than an indication of the emissions to be expected. The emission factors are based on weight percentages. For lack of (measurement) data no statement can be made about the asbestos type and the form of the asbestos, bound or in coarse or fine fibres.

Asbestos cement

- Production

Solid waste arises during the cutting to size of the material, from production faults and from the dust collected in the cloth filters. The total solid waste volume is 2.5 ktonnes a year, 1.5 ktonnes of which are

recycled. This waste contains 9% asbestos, or 90 tonnes.

In addition, there is waste in the form of sludge from the sedimentation basins. Asbestos-cement slurry that cannot be processed because of disruptions in the process is also dumped in these basins. Ten ktonnes of sludge are involved per year, with about 10% solid matter containing 10% asbestos (Van der Ven, 1984). Some 100 tonnes of asbestos are disposed of annually with this waste.

Emissions into water occur as a result of the water withdrawn at the screens. Industrial water from other sources also contains small amounts of asbestos. The emission in 1982 was 350 kg. In the meantime, this has been reduced to less than 10 g per year as a result of virtually complete recirculation of the process water (as reported by the producer).

The only remaining source of emissions into the air is the cutting to size of the manufactured sheets. The total emission into air is 0.3 kg per year (as reported by the producer), giving an emission factor of less than 0.1 g per tonne.

- Processing

During the processing of asbestos cement, waste arises from breakage, material that is no longer usable and dust from the cloth filters (about 0.5% of that portion of the asbestos cement still requiring pretreatment). Emission into the air will occur especially during the cutting to size of sheets, and the punching and milling of holes.

The following information was used for the calculation of the emissions. Asbestos cement products are usually cut to size beforehand in a central workshop; only about 20% of the operations will be carried out on the construction site. When asbestos cement is processed at supply companies, an exhaust with a filter system will be present, but not when it is handled on the building site. It is estimated that 15% of the asbestos cement (total 17.8 ktonnes, with 12.5% asbestos) will still be processed on site (80% in a workshop and 20% on the construction site). Without a filter, the emission will be 1 kg dust per tonne of asbestos cement processed, and 1 g per tonne with a filter. The dust generated is collected in a filter, turning it into solid waste. Because of a 5% loss, 890 tonnes of solid waste of asbestos cement are produced, containing about 110 tonnes of asbestos. The processing plants emit about 1.8 kg asbestos into the air per

year and the construction sites about 445 kg. The captured dust contains about 1.8 tonnes of asbestos.

- Use

During the use of asbestos cement in the form of sheets, pipes and roofing, fibres will be set free because of weathering, erosion or wear. Measurements indicate that new material releases up to 10 times more fibres than old material (Lanting and Den Boeft, 1979; Spurny et al., 1980). Rainwater coming from new roof material will consequently contain more fibres than rainwater running down older roofs. Part of this asbestos will be removed via sewers and part will find its way into the soil. It has been assumed that the amount released into the air by wind, erosion, walking on roofs and dissemination of fibres from dried rainwater will be of the same order of magnitude as the amount washed away by rain.

It is estimated that about 75 ktonnes of new asbestos cement are used outdoors per year (about 7.5 mln m^2). The surface area accumulated over the years in outdoor applications is 360 mln m^2, giving rise to 60 kg asbestos being washed away, and of 60 kg being released into the air each year.

About 40% (35,600 km) of the drinking-water network consists of asbestos-cement pipes. Drinking water contains on average 0.2-2 mln fibres.l^{-1} (Commins, 1984). It is assumed in the literature that only part of this is derived from the pipes. This indicates that the release of asbestos fibres from pipes is of the same order of magnitude as that from asbestos sheets and roofing.

The total length of asbestos-cement waste-water pressure pipes in the Netherlands is less than 2,500 km. Assuming that the amount of fibres set free as a result of weathering is similar to that for drinking-water pipes, then its contribution to the emission into water is very small.

It should be noted that under conditions corrosive to cement, especially in an acid environment, the emission of fibres can be much greater. This will hardly ever occur in the Netherlands.

- Removal and demolition

Asbestos cement, used in durable applications, house-building and pipe systems, will be released as waste during demolition or renovation work. This material is not reused directly. Emission into the air and possibly water occurs as a result of the handling and breaking up of the material on the demolition site. The useful life of dwellings and pipes is estimated to

be 50 years or more. It is further assumed that since 1940 about 80% of the asbestos has been used in the construction industry. On the basis of this information, SVA (1978) has estimated that in 1982 about 1.6 ktonnes of asbestos was present in building and demolition waste in the form of asbestos cement, that by the year 2000 this will be about 5 ktonnes and that from 2030 the asbestos in this waste stream will be as much as about 245 ktonnes. The total waste stream of asbestos cement will then be some 200 ktonnes per year from the demolition and renovation of buildings, pipe systems, etc.

The amount of dust released during the breaking up of asbestos cement is estimated at 1 kg per tonne. Part of this will actually be emitted into the air as dust (about 0.1 kg per tonne); around 155 kg of asbestos are estimated to have been emitted in 1982. This estimate is not based on measurement data and the actual emission could have been a factor of 10 higher or lower. Neither the nature of the emission nor the distribution between free and bound asbestos fibres are known. An emission of 200 kg per year is provisionally accepted.

- Rubble breaking

Part of the construction and demolition waste - which also contains material from broken-up roads - is reduced in size and screened. This material is again incorporated into road foundations and sometimes concrete. There are a total of 63 rubble-breaking plants in the Netherlands, which handle about 3,400 ktonnes of rubble annually; this is about 55% of all construction and demolition waste. In this process, 1-4 kg of very fine dust per tonne is released (DHV, 1985). Part of this, an estimated 0.1 kg per tonne, will actually escape into the air as dust emission, assuming that the rubble is wetted down.

Only un-"contaminated" rubble is processed in principle. Rubble is usually presorted at the source. It is not known to what extent this affects the occurrence of asbestos cement in the material to be broken up. If the composition of the dust released is representative of the construction and demolition waste as a whole (thus 230 g per tonne), then the estimated total emission of asbestos into the air is around 80 kg per year.

- Summary of emissions from asbestos cement

The emissions occurring as a result of the production and use of asbestos cement are summarized in table 2.7.

Table 2.7. Summary of the estimated amounts of asbestos in emissions and waste derived from asbestos cement in the Netherlands in 1982

Source	Emissions (asbestos) Air (kg/yr)	Water (kg/yr)	Waste (kg/yr)	In waste (%)	Total solid waste (tonnes/yr)
Production					
-cloth filters + loss	0.3		90	9	1,000
-water purification		350*	100	1	10,000
Primary processing					
-cloth filter (companies)	2		2	12.5	14
-on building sites	445		-		-
-loss			110	12.5	890**
Weathering					
-building materials	60	60	-		
-pipes	-	<0.05	-		
Demolition/replacement					
-buildings	200***		1,560***	-	-
Rubble breaking	80	n.a.	-		
Total	787	410	1,862		

* has meanwhile been cut to 10 g per year
** found mostly in construction and demolition waste
*** can rise sharply in the coming 50 years

Brake linings, brake pads and friction material

- Production

In the production of brake pads, asbestos fibres are mixed with synthetic materials. This mixture is compacted on steel plates and hardened onto them. After this hardening, the parts are machined. The principal sources of emissions into the air are the unpacking of the fibres and the mixing of them with the resin components. Only minute amounts of fibres will be released during the grinding and drilling processes.

Asbestos-silicone yarns are the base material for the manufacture of friction materials for clutches. These are soaked in mixtures of synthetic resin, metal powders and rubber. This is then wound, compacted and vulcanized, followed likewise by grinding and drilling. Solid waste is made up of rejected products, collected dust and residues from milling, grinding and sawing. This production waste is about 12.5% (Lanting and Den Boeft, 1979), yielding 320 tonnes of waste containing about 110 tonnes of asbestos in 1982.

The principal source of emission into the air is the unwinding of the asbestos yarn and the finishing processes in the manufacture of the above-mentioned materials: an emission of around 300 kg per year.

- Use and maintenance

Asbestos fibres can be released through wear when friction and braking materials are used. The Dutch fleet of cars is by far the most important source of this emission. The estimated total emission from brake linings and friction materials is around 1,700 tonnes a year (DHV, 1984). Under the conditions prevailing during wear, the asbestos disintegrates, depending on the speed at which the car is braked. Rödelsperger et al. (1985) reported that the dust released contains on average 0.25% asbestos. This means that about 4,250 kg asbestos are released annually, consisting of short and long chrysotile fibres (average aspect ratio is 23). Part of this asbestos falls directly on the road, part remains behind in the brake lining and the rest is emitted into the air. On the basis of immission measurements, the emission into the air is estimated at 600 kg per year (Lanting and Den Boeft, 1979). The remainder (about 3,650 kg per year) will be released chiefly during maintenance work on the brakes. It may be assumed that maintenance of the brakes is carried out without special precautions. Exhaust systems have been installed in only a limited number of large maintenance shops. Part of this brake dust is relatively coarse and will not become airborne. It is assumed that about 10% is dust and is emitted into the air (365 kg per year). The remainder of the asbestos dust present in the workrooms (about 3,3 kg per year) will be disposed of with the other garage waste.

- Replacement

Worn-out braking and friction materials are replaced. The total amount of waste released annually will be equivalent to the sum of production and net imports minus wear. The material is replaced when about 60% has worn away. This generates annually 1,130 tonnes of waste containing about 400 tonnes of asbestos. The asbestos in this waste is very tightly bound so that emissions into the air resulting from the handling of the material during replacement are insignificant. The emission resulting from accumulated brake dust has been included in the estimate of the dust emission caused by usage.

- Summary of emissions from braking and friction material

Table 2.8. summarizes the emissions occurring from the production and use of asbestos-containing braking and friction materials.

Table 2.8. Summary of the estimated amounts of asbestos in emissions and waste derived from asbestos-containing braking and friction materials in the Netherlands in 1982

Source	Emissions			In waste	Total solid waste
	Air (kg/yr)	Water (kg/yr)	Waste (kg/yr)	(%)	(tonnes/yr)
Production	300	-	110	ca.35	320
Use					
-on the road	600	-	-		
-in garages	365	-	3.3	0.25	n.s.
Replacement					
-waste	-	-	400	ca.35	1,140*
Total	1,265	-	513		

* will end up in a much larger waste stream

Insulating, packing and sealing materials

- Production

In 1982, only asbestos felt and paper were still produced in the Netherlands; this production has been discontinued since 1982.

- Processing

Asbestos paper, millboard, felt, etc. are both used directly and incorporated into other products, such as gaskets. Asbestos cord and braided material are also used for sealing and insulation. The asbestos content in these products varies between 50% and 90%. Waste arises when these materials are cut to size and formed into blanks as well as from processing faults, and can vary between 5% and 30% depending on the application. The varying extent to which asbestos is bound in the products also causes wide variation in the emission into the air, which is estimated to be between 0.01 and 0.1 kg per tonne.

- Maintenance and demolition

It is assumed that there is virtually no increase in the usage of these materials. The waste created by maintenance work and replacement of gaskets and the like can then be equated to the sum of net imports and production.

- Summary of insulation and packing materials

Table 2.9. summarizes the emissions occurring as a result of the production and use of asbestos-containing insulation and packing materials.

Table 2.9. Summary of the estimated amounts of asbestos in emissions and waste derived from asbestos-containing insulation and packing materials in the Netherlands in 1982

	Emissions			In waste	Total solid waste
	Air (kg/yr)	Water (kg/yr)	Waste (kg/yr)	(%)	(tonnes/yr)
Production*					
-cloth filters	20	-	2	80	3
-water purification	-	200	7	5	140
-loss	-	-	50	80	62
Processing					
-scrap	-	-	150	80	190
-filters	54	-	5	80	6
Replacement/demolition	54	-	800	70	1,150**
Total	128	200	1,014		

* ceased after 1982

** will end up in a much larger waste stream

Asbestos-containing bitumen, coatings, mastics, concrete adhesives

-Production

In the production of these materials, asbestos is loosened and mixed with bitumen and fillers. Emission into the air occurs during the loosening and mixing of the asbestos. The emission is limited because of the precautions taken. Solid waste is made up of a small amount of production loss (1%) and the dust collected in the filters (0.1 kg per tonne). The emission factor for emission into the air (after passage through a filter) is 0.001 kg per tonne (ERL, 1982). This is also so low because of the low concentration in the product and the tight bonding.

- Processing

Solid waste consists of product residues present in cans and the like. The amount of waste (residues and from processing faults) is estimated to be 5%. Because of the low concentration and tight bonding, emission into the air during use of the products will be small (0.01 kg per tonne).

- Use

Because of the strong bond and low concentration, the emission of asbestos fibres from wear and processing will be small.

- Demolition

The bulk of the asbestos is present in bitumen for roofs. Its useful life will be about 15 years. The same is true for its use in tile adhesives. Concrete adhesives will probably last much longer. On the basis of the current quantities in existing buildings (table 2.5.), the waste stream generated annually will be some 600 tonnes of asbestos. The emission into the air from demolition is small, an estimated 0.01 kg per tonne.

- Summary of mastics, bitumen, etc.

Table 2.10. summarizes the emissions resulting from the production and use of asbestos-containing mastics, bitumen and the like.

Table 2.10. Summary of the estimated amounts of asbestos in emissions and waste derived from asbestos-containing mastics, bitumen, etc. in the Netherlands in 1982

Source	Emissions		Waste	In waste	Total solid
	Air	Water			
	(kg/yr)	(kg/yr)	(tonnes/yr)	(%)	(tonnes/yr)
Production *, loss			3	3	100
filters	0.3	-	0.3	3	10
Processing	7	-	35	ca.3	1,150
Demolition	6	-	600	little	**
Total	13.3	-	638		

* *significant part in bitumen for roofs*

** *ends up in part in construction and demolition waste*

Floor coverings

- Production and use

It concerns two types of floor covering: floor covering on a roll with an asbestos-paper/-felt backing, and asbestos-containing vinyl tiles. The tiles are imported. The linoleum floor covering backed with asbestos was produced in the Netherlands up till 1983, using asbestos felt produced elsewhere in the manufacturing process. The two types of floor covering contributed about 170 tonnes of asbestos to the total consumption in the Netherlands.

- Processing

The total surface area of asbestos-containing floor covering laid annually was in 1982 about 160,000 m^2 of felt-backed floor covering and about 227,500 m^2 of vinyl asbestos tiles. Some asbestos is released during the

laying of the floor covering, especially the type with an asbestos-felt backing. The actual emission into the air is estimated at 0.0001 kg per tonne for vinyl tiles and 0.1 kg per tonne for the felt-backed floor covering. Solid waste arises as a result of loss in cutting the material to size, etc. This loss is greater with floor covering on rolls than with tiles (estimated at 5% and 1% respectively).

- Use

The current surface area of asbestos-containing floor covering laid in buildings is 7 to 10 million m^2 of floor covering backed with felt and about 1 million m^2 of vinyl asbestos tiles (table 2.5.). Emissions occur as a result of wear and damage. It is assumed that the average wear is 1% over a 10-year period. The greater part of the released material will remain on the floor. Part of this will be removed as dry dust and some will end up in water as a contaminant during wet cleaning (50% each). The emission into the air is estimated to be 0.1% of the released material.

- Replacement and demolition

Floor covering backed with felt has a shorter life than vinyl asbestos tiles. An average of 10 years may be accepted for the former, and 20 years for the latter. This would give rise to 1150 tonnes of waste per year from the currently accumulated amount of floor covering. As with asbestos cement, it will take years before this level is reached. The waste stream was about 170 tonnes in 1982. A substantial portion of this waste will end up in domestic refuse, and a portion in construction and demolition waste. A relatively large emission could occur during the removal of floor covering, consisting of accumulated dust and of dust derived from sanding floors which have remnants of attached floor covering (an average of about 0.05 kg per tonne for all types of floor covering).

- Summary of floor coverings

Table 2.11. summarizes the emissions resulting from the production and use of asbestos-containing floor coverings.

Table 2.11. Summary of the estimated amounts of asbestos in emissions and waste derived from asbestos-containing floor covering in 1982

Source	Emissions			In waste	Total solid waste
	Air (kg/yr)	Water (kg/yr)	Waste (tonnes/yr)	(%)	(tonnes/yr)
*Production **					
- waste			*7*	*8*	*9.0*
- cloth filter	*1*		*1*	*8*	*12*
Processing	*3.5*		*3*	*ca.15*	*20*
Use	*2*	*900*	*1*	*little*	*88*
Demolition	*8.5*		*170*	*ca.15*	
Total	*15*	*900*	*182*		

* *has fallen sharply since 1982, and has now ceased*

** *ends up in part in large waste streams (construction and demolition waste)*

Electrolysis diaphragms

In the manufacture of chlorine by electrolysis, a diaphragm is used consisting of a hollow perforated cathode coated with asbestos. In the Netherlands, the diaphragm electrolysis process takes place at one location. Emissions occur during several stages in the process of cathode renewal: dust during mixing, fibres in the waste water, and solid waste during the removal of asbestos residues from the spent slurry. In addition, the old diaphragm constitutes a solid waste which has to be disposed of. In 1982, total solid waste was 30 tonnes, emission into water 1,200 kg and that into air about 250 g. These emissions have meanwhile been cut: in 1986, 22 tonnes of solid waste were produced and 240 kg of asbestos were emitted into the water and 50 g into the air.

Liquid filters

Special filters are employed in the filtration of liquids in the food and pharmaceuticals industries to remove pathogenic organisms. A specific type is made of asbestos-fibre-reinforced cellulose. Asbestos fibres can be released during its use. The estimated emission of asbestos into the filtered liquids is 0.01% (Spurny et al., 1981) (0.044 kg per year), which will eventually enter the environment. The emission resulting from installation and cleaning of the filters will only be minimal. The total import of 2 tonnes of asbestos-bearing filters, containing 440 kg asbestos, will be consumed annually and will thus have to be disposed of as solid waste.

Insulation

The use of asbestos for insulation is no longer permitted. The amount of asbestos in this application (insofar as still present) is estimated to be 5,000 tonnes (De Vos, 1981). The bulk of this is sprayed asbestos, which is still present in at least 200 buildings (Tempelman et al., 1985). The total surface area is around 100,000 m^2 (Anthonissen et al., 1985). Emissions occur as a result of air movement past the layers, maintenance work, etc. Because of the measures already taken, the emission will be limited to about 0.001 kg per tonne, a total of 5 kg per year. Demolition work will also give rise to emissions despite all the measures taken, estimated at 0.01 kg per tonne. It is expected that in the course of the coming 10 years most of the sprayed asbestos will be removed. This implies that during this period 5 kg asbestos will be emitted into the air each year as a result of the demolition of insulating asbestos.

2.2.3. Secondary emissions

Asbestos-containing waste and waste-water streams arise from emissions into soil, water and air, the generation of waste materials and the exchange between them. Their treatment leads again to emissions and waste streams.

Waste incineration

In the Netherlands, part of the waste is incinerated. Industrial waste which specifically contains asbestos will be dumped. Household waste, however, also contains asbestos. The asbestos content of domestic refuse in 1976 has been estimated at 750 $mg.kg^{-1}$ (SVA, 1978; Anthonissen et al., 1985). As a result of the reduced usage of asbestos, certainly in domestic appliances and materials, this will have fallen. The use of asbestos has decreased by roughly a factor of 10 since 1976. It is assumed that there will have been a similar reduction in the asbestos content of domestic refuse.

In 1982, about 2,500 ktonnes of the 4,900 ktonnes of waste were incinerated. Incineration causes asbestos to be released into the air together with the flue gases on the one hand, and in the form of a solid waste stream of collected fly ash and slag on the other. A small amount will also be emitted into water when the wet slag removal process is

employed. For every tonne of waste burned, 5500 m^3 of waste gases are emitted, containing 150 mg of dust per m^3 (Anthonissen et al., 1985). Assuming that the solid fraction of the waste (25%) contains 240 mg asbestos.kg^{-1}, that the fly ash and slag have a similar asbestos content, and that 90% of the asbestos is degraded in the waste incinerator, then 50 kg of asbestos will be emitted into the air per year. Eighty-three ktonnes of fly ash, containing 2 tonnes of asbestos, are dumped and 625 ktonnes of slag containing 15 tonnes of asbestos.

Dumping of waste materials

For asbestos-containing industrial waste with ≥ 5 g asbestos per kg waste to be admitted, waste disposal sites must be exempted under the Chemical Waste Act. At present, 6 waste dumps in the Netherlands have been granted such an exemption. A survey conducted in 1983 (Kaper, 1984) showed that at least 8 dumps received asbestos-containing waste. This limit does not apply to domestic refuse.

In what form the asbestos is bound and how the waste is supplied and dumped are important in determining the resulting emission into the air.

Lanting and Den Boeft (1979) estimated the emission to be 0.1 kg per tonne when asbestos cement waste is dumped. This is now generally believed to be too high a value, so that an emission factor of 0.01 kg per tonne has been used here. For waste containing almost 100-per-cent unbound asbestos, the same emission factor of 0.01 kg per tonne is considered to be realistic in view of its careful handling.

Large waste streams with asbestos will be handled less carefully on the one hand, but contain little asbestos on the other. An emission factor of 0.01 kg per tonne has also been used for this.

The total volume of about 4500 tonnes (see table 1.12.) of asbestos in the aforementioned categories of waste will cause approximately 45 kg to be emitted into the air per year.

Drinking water supply

Surface water will contain a certain concentration of asbestos fibres. Part of the fibres will enter the drinking water during the preparation of drinking water from surface water, and part remains behind in the sludge produced during water purification. About 30% of the drinking water (349

mln m^3) was obtained from surface water in the Netherlands in 1982. Its purification produces about 19 ktonnes of sludge per year. Most of this sludge is dumped at or outside the site of origin (Koppers, 1982). Its asbestos content depends on the concentration of asbestos fibres in the surface water. There are no measurements of this available for the Netherlands. The asbestos level in the sludge could be about 100 to 200 ppm, assuming a fibre concentration of 10 mln fibres per litre in Rhine water (Lawrence et al., 1975).

Waste water treatment

The purification of waste water is comparable to that of surface water for potable water. The primary and secondary sludge produced will contain asbestos fibres. The content of asbestos fibres of normal waste water, and therefore also the potential concentration of asbestos in sludge, is not known. The total sludge output from waste-water treatment in the Netherlands is about 2,500 ktonnes per year (dry matter content is 5-15%). Soil and surface water may become contaminated when sludge is dumped or processed (e.g. into black earth or compost). The incineration of sludge can give rise to emission into the air of flue gas contaminated with asbestos.

2.2.4. Uncharacteristic diffuse sources

Asbestos fibres can be released during the processing and use of substances and materials which contain asbestos as an (adventitious) component or contaminant.
Asbestos cement waste has been used in the past for paving yards and country roads (several hundreds of tonnes; Hennekam et al., 1984). Construction and demolition waste has been used more indirectly as filling material in the construction of roads, dams and (noise) barriers. Use of the waste in open applications, in particular, can give rise to emissions into the air through dissemination. In addition, ground- and surface water may become contaminated.
Emissions can also occur during the breaking and sorting of construction and demolition waste (table 2.7.) and the processing of waste sludge, from compost made from domestic refuse, and during the spraying of tap water (which can contain up to one million asbestos fibres per litre) in air

conditioning systems, for example (Lanting and Den Boeft, 1979; Commins, 1984).

The use of rocks and minerals containing naturally small quantities of asbestos can also lead to emissions. Examples are:

- serpentine rock types for paving roads.
  As far as is known, they are not used for this purpose in the Netherlands.
- talc.
  It is assumed that most of the talc types processed in the Netherlands do not contain asbestos. As far as is known, only limited amounts of asbestos-containing industrial talc are still imported. It is also not known to what extent imported talcose products contain asbestos-bearing talc.
- ores, especially iron ore.
  Asbestos can be present in crude iron ore from specific localities. The ores processed in the Netherlands, however, are pre-sorted ores and concentrates. As far as is known, these are asbestos-free.
- absorbents.
  Porous material used for removing spilled oil and the like as well as the material intended for cat-box litter can contain asbestos. It concerns absorbents made from natural (mostly vulcanic) rock. As far as is known, the absorbents used in the Netherlands, attapulgite, zeolite and sepiolite, do not contain asbestos.

2.2.5. Emissions in foreign countries

The production and consumption patterns of asbestos-containing components in neighbouring countries are similar to the situation in the Netherlands. Asbestos consumption in the EEC for use in asbestos cement was 439 ktonnes in 1978. Assuming a similar trend to that in the Netherlands in the total consumption of asbestos, this would have been about 250 ktonnes in 1982. With an overall emission factor of around 0.05 kg per tonne for the total consumption of asbestos cement, this means that the resulting emission into the air (from the use of asbestos cement) in all EEC countries was about 13 tonnes in 1982.

Assuming that car use in the EEC does not differ from that in the Netherlands, then the asbestos emission in the EEC from the production and use of braking and friction materials is estimated at 21 tonnes per year.

This is based on a fleet of motor vehicles in the EEC of 92 million and an emission factor of 0.23 g per vehicle per year.

2.2.6. Emission factors and characteristics

The proportion of asbestos in the emissions can vary widely. The emission often originates from several process steps. The final emission is then made up of various primary emissions which will not all contain asbestos (e.g.: when an exhaust has been fitted over a saw for asbestos cement, some dust from the workplace will also be removed, as well as asbestos cement). Consequently, with most emissions it is not possible to establish a direct relationship between total dust emission and asbestos emission. The emission factors used are partly based on literature data. When no values were found in the literature, values which, incidentally, are usually also based on estimates, an emission factor was estimated from a comparison with known emissions, taking into account the asbestos content, the extent to which asbestos is bound, and any measured particle concentrations in the immediate vicinity of such a source, known from the literature (Commins, 1985; Timmerman, 1984).
Another basis for emission factors is the useful life of a product and its anticipated wear. Both depend on the application of the product. The emissions mentioned, especially those into the air, are therefore no more than rough indicative values. It has been assumed that chemical or thermal degradation of asbestos fibres does not occur, unless clear indications exist to the contrary.

Asbestos fibres are usually bound to a matrix. In only a few products, such as fabric and cord, etc., is asbestos not bound and sometimes the degree of bonding is very low (as with sprayed asbestos materials). In the case of emission into water, involving finely divided material, a significant part of the emission will consist of free fibres. These are fibres not yet bound or fibres which have become dislodged from the matrix as a result of processing or wear. In emissions into the soil, in the form of waste, the asbestos is bound in exactly the same way as in the product from which it is derived. Here, the possibility exists that asbestos fibres are set free as a result of mechanical treatment or weathering, and are then emitted into air or water. The main fraction of the fibres being released consists of fibres with a length of less than 0.5 to 1 μm. It is impossible to

predict what percentage this would be of the total asbestos emission. Chrysotile particles are generally smaller than amphibole ones. In addition, both the pretreatment during production and the prevailing conditions during fibre release are important. For example, the residual emission after an appropriate emission-control technique will consist entirely of very fine fibres. Sixty per cent of the emissions from the wear of asbestos cement are fibres with a length of < 5 μm (Spurny et al., 1985), whereby it should be noted that larger fibres can disintegrate into smaller ones through weathering.
Only chrysotile is still processed in the Netherlands (subsection 2.1.2.). In the case of emissions resulting from older applications, however, crocidolite and amosite can be released. It is almost impossible to determine how large the average annual emission of these fibres is, both because these fibres have not been used for some considerable time and the useful lives of the various products differ so widely. Furthermore, it will only be a small percentage of the total emission of asbestos (< 5%), in view of its use in the past. However, these emissions locally can be large (especially where sprayed asbestos materials have been used).

2.3. SUMMARY AND CONCLUSIONS

Asbestos-bearing rock is quite common in Europe, but does not occur in the Netherlands. The products from weathering of this rock could make a very small contribution to concentration levels in our country.
Of the world production of raw asbestos of nearly 4000 ktonnes in 1982, the Netherlands imported over 5 ktonnes. The net import of asbestos amounted to over 15.5 ktonnes.
The number of applications has decreased drastically as a result of statutory measures; total consumption has also fallen. In the past, other types of asbestos, amosite and crocidolite, were used in only a limited number of products. The form in which asbestos is released differs for each environmental compartment. Emission into the soil occurs chiefly as a result of the dumping of waste materials. Much of the solid waste containing asbestos is generated at a specific locality and is removed separately. The form in which asbestos is present, free or (tightly) bound, and the concentration of asbestos in the total waste stream determine its processability and any possible secondary emissions. Table 2.12. summarizes the waste streams, divided into three types of asbestos-containing waste

streams: (practically) unbound asbestos, bound asbestos and free or bound asbestos as a fraction of a large waste stream. Soil contamination also occurs as a result of deposition and infiltration; however, this is only a small fraction of the total asbestos load in the soil.

Table 2.12. Asbestos in waste in 1982

Waste type	*Asbestos in waste stream (tonnes/yr)*	*Asbestos in waste stream (%)*	*Total waste stream (tonnes/yr)*
(practically) Unbound asbestos in waste from:			
- removal of sprayed insulation	*500*	*80*	*625*
- production of insulating materials	*50*	*80*	*62*
- replacement of electrolysis diaphragms	*30*	*ca.100*	*30*
Total	*580*		*717*
Bound asbestos in waste from:			
- demolition/replacement of insulation, paper, millboard, packings, etc.	*800*	*70*	*1,150**
- replacement of braking and friction materials	*400*	*35*	*1,140**
- replacement of asbestos-cement pipes	*200*	*17.5*	*1,200**
- asbestos cement production	*190*	*1/9*	*10,000/1000*
- removal of floor covering	*170*	*ca.15*	*1,150**
- processing of packings, paper, millboard, insulation, etc.	*150*	*70*	*215*
- production of braking and friction materials	*110*	*35*	*320*
- processing of asbestos cement	*110*	*12.5*	*880**
- use of cloth filters (total)	*45*	*ca. 5*	*950*
- production and processing of bitumen, mastics, coatings	*38*	*3-10*	*1,180*
- waste water (sludge) from production of packing and insulating materials	*7*	*5*	*140*
- production of floor covering	*7*	*8*	*90*
Total	*ca.2,230*		*ca.24,000*
Asbestos in large waste streams:			
- construction and demolition waste	*1,560*	*-*	*-*
- domestic refuse incineration: slag, fly ash	*17*	*24 ppm*	*710,000*
- industrial waste	*3*	*very low*	*-*

** this will end up in part in other very large waste streams such as construction and demolition waste, scrap, etc.*

The emissions into water and air will involve both free and bound fibres. However, fibres still bound will only be emitted or directly deposited to a limited extent as a rule. The asbestos released into water and air is in most cases a small part of a much larger dust emission. Direct emissions into water occur in only a few cases, usually resulting from wet production

processes. In addition, large diffuse emissions occur during the wet removal and rinsing of fibres, produced by weathering and wear (e.g. of asbestos-cement corrugated sheets and floor coverings). Table 2.13. lists the sources in order of size.

Table 2.13. The principal asbestos emissions into water in 1982

Emission from:	*Emission (kg/yr)*	*Contribution to the total annual emission (%)*
- *installation of electrolysis diaphragms*	*1,200**	*44*
- *weathering of floor covering*	*900*	*33*
- *production of asbestos cement*	*350***	*13***
- *production of packings, insulations, etc.*	*200*	*7*
- *weathering of asbestos cement (outdoors)*	*60*	*2*
Total	*2,710*	*100*

* *since 1986, 240 kg per year*
** *has meanwhile decreased to 0.01 kg per year*

The total emission into the air comprises a number of highly localized sources, chiefly from production processes and several very diffuse sources. Table 2.14. lists the principal sources in order of size. In the case of the diffuse emissions, the amount of both the dust emission as such and the asbestos emission is difficult to estimate, if at all. In addition to the primary sources mentioned, re-emission of fibres contributes to the asbestos fibre load in the ambient air in particular (subsection 3.3.2.). Its magnitude cannot be estimated at the moment.

Table 2.14. The principal asbestos emissions into the air in 1982

Emission from:	*Emission (kg/yr)*	*Contribution to the total annual emission (%)*
- *brake dust on roads*	*600**	*26*
- *production of braking and friction materials*	*300**	*13*
- *demolition of buildings, rubble breaking*	*280**	*12*
- *brake dust in garages*	*365**	*16*
- *weathering of asbestos-cement building materials*	*60**	*3*
- *processing of asbestos cement on site*	*445***	*20*
- *processing of insulation, packings, etc.*	*54***	*2*
- *demolition/replacement of insulation, packings, etc.*	*54***	*2*
- *household waste incineration*	*50***	*2*
- *dumping of waste*	*45***	*2*
- *production of insulation, packings, etc.*	*20***	*1*
Total	*ca 2275*	*100*

* *consists largely of loose asbestos fibres*
** *consists chiefly of bound asbestos*

3. DISTRIBUTION AND CONVERSION

3.1. BEHAVIOUR IN THE SOIL

Asbestos fibres are extremely resistant to chemical degradation and consequently remain in the soil for some considerable time. The asbestos present in the soil in the Netherlands will be derived chiefly from the dumping of asbestos(-containing) waste. Commins (1979) stated that (unbound) asbestos fibres can seep through thin layers of soil. In this way, asbestos(-containing) waste dumped on waste disposal sites can come into contact with the groundwater and subsequently surface water. According to Commins (1979), the extent of this transport of (unbound) asbestos fibres is limited; the greater part of the asbestos waste is bound to a matrix of cement, plastic or resin, so that transport is greatly impeded.

3.2. BEHAVIOUR IN SURFACE WATER

Asbestos fibres are inert and consequently remain in water for a long period of time and can be dispersed over long distances. Suta and Levine (1979) stated that asbestos fibres can be transported via water over hundreds of kilometres.

3.3. BEHAVIOUR IN AIR

3.3.1. Distribution

As regards the nature and location of the sources from which asbestos is dispersed in the Dutch atmosphere, the following distinction can be made:
- permanent and incidental sources;
- static and mobile sources;
- many small and a few large sources.

This characterization can be used to estimate on which scale each of the emissions mentioned in chapter 2 is followed by a rise in the asbestos concentration.
Local increases may be expected near permanent static sources, the principal ones in the Netherlands being the manufacturing plants of asbestos cement, braking and friction materials, bitumen and coatings, as well as the domestic waste incinerators. In

addition, local increases in the air can occur in areas with asbestos road paving as a result of re-emission (subsection 3.3.2.).

In the case of an incidental source, for example, the handling of asbestos products or the demolition of asbestos-containing installations or buildings, the distribution of asbestos will be of a temporary nature. It will, however, not be restricted to the duration of the activity, since asbestos residues can disperse in the air hereafter (re-emission). With this type of source, the distribution depends heavily on how carefully the work is carried out, how the asbestos was or is being applied, and how the material is transported. Calculations of the anticipated concentration levels cannot therefore be made without this information. Moreover, there is the problem of how any calculated temporary rise in concentration can be translated into an excessive inhaled dose.

Mobile sources (the wearing of friction materials) can give rise to an increase in concentration of long duration when there are many of these sources in a limited space. Road traffic belongs to this category. As regards the other sources, the distribution of asbestos in the Netherlands is of a diffuse nature, so that the following levels can be distinguished:

- national level (area cross section up to a few hundred km);
- urban level (area cross section up to a few dozen km);
- local level near static sources (area cross section up to a few km);
- road/street level (area cross section up to a few dozen metres).

The reliability and accuracy of the results are determined chiefly by those of the emission data. The emission factors employed are usually based on estimates (subsection 2.2.6.), so that more knowledge needs to be amassed about the emissions, especially when there is a discrepancy with measurement results.

Since the calculations were made on the basis of the emissions mentioned in chapter 2, the respective contributions will also be expressed in concentrations ($ng.m^{-3}$). The relevance of these values for a possible risk assessment will be discussed in more detail in chapter 5.

Distribution on a national scale

The total emission of asbestos into the air in the Netherlands was about 2 tonnes in 1982 (see table 2.14.), which originated almost exclusively from diffuse sources. It was deduced from calculations on NO_2 and SO_2 (Van Egmond and Huygen, 1979; Van den Hout et al., 1983) that the concentration contribution per 1000 tonnes of emissions is about 0.04 $\mu g.m^{-3}$. This works

out at an asbestos concentration of 0.09 ng.m^{-3} on a national scale. The contribution made by the sources in the neighbouring countries was estimated, assuming a typical residence time of 1 month for asbestos (subsection 3.3.2.). Furthermore, the assumption was made that the emission per head of population in these countries is the same as that in the Netherlands. The concentration contribution from Belgium and West Germany is 0.03 ng.m^{-3}, that from the rest of Western Europe within a distance of 800 km 0.02 ng.m^{-3}. The total large-scale concentration of asbestos in the Netherlands is by these estimates thus 0.14 ng.m^{-3}. This value is of limited significance where it concerns the respirable fraction. If 1 ng equals 2,000-40,000 fibres, this means a large-scale concentration of 400-8,000 fibres per m^3. This value is of the same order of magnitude as that deduced from the measurements (subsection 5.4.2.). The influence of re-emissions was not taken into account for lack of data. However, it is possible that this re-emission (especially on a large scale) makes no small contribution to the asbestos concentrations.

Distribution on an urban scale

The greater part of the emissions occur during or as a consequence of man's activities. Therefore, an estimate was made of the concentration levels in urban areas, assuming that these levels are proportional to the population densities.

In the 21 urban conurbations in the Netherlands with over 100,000 inhabitants each, representing 46% of the total population and covering 15% of the land area, the average population density is about 5 times higher than in the rest of the Netherlands and 3 times the national average. It can be calculated from this that the concentrations on an urban scale are on average 0.3-0.4 ng.m^{-3}. These are roughly the same as the measured values (see table 5.4.).

Distribution on a local scale

On the basis of the permanent sources listed in table 2.14. (manufacturing companies, domestic waste incinerators), the contribution to annual average concentrations in the vicinity of a source emitting 10 kg per year was calculated using the National Model (not taking into account small deposition losses). The results of this calculation are shown in figure 3.1. The contribution is about 2 ng.m^{-3} at a distance of 200 m, about 0.5

$ng.m^{-3}$ at 500 m and about 0.2 $ng.m^{-3}$ at 1 km. These values are somewhat lower than those being measured near industrial sources (see table 5.4.). In addition, local increases in concentration can be caused by dispersion during and after demolition work. It can be inferred from chapter 2 that this activity accounts for about 15% of the asbestos emission in the Netherlands. Since the magnitude of several important parameters (number of buildings, quantity of asbestos, mode of attachment, manner and duration of demolition) may differ widely from case to case and are usually not known, a reliable estimate of the concentration increase cannot be made in advance. However, it may sometimes be possible, with a few presuppositions, to estimate an order of magnitude. As regards the total quantity of sprayed insulation in place (5000 tonnes), it may be presumed that this quantity is equally divided over twice the number of buildings that are known to contain asbestos (at least 200) (Tempelman et al., 1985); an average of about 12 tonnes of sprayed asbestos will then be removed per object during demolition. At an emission factor of 0.01 kg per tonne, this means an average emission of 0.12 kg per object demolished. If this amount is released within one workweek (40 hours), then the average source strength during demolition is 0.003 kg per hour. This emission seems larger than that from the above-mentioned permanent source of 10 kg per year (about 0.001 kg per hour), but will not recur at the same site; total exposure of the population in the neighbourhood will, on balance, be small. On the other hand, the demolition workers will receive a much larger load.

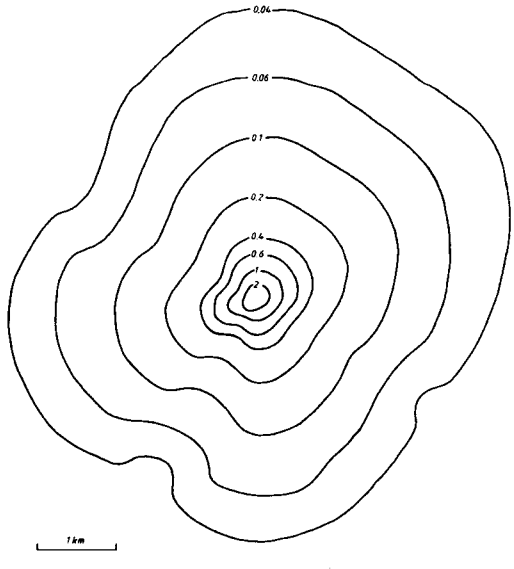

Figure 3.1. Annual average concentrations (in $ng.m^{-3}$) of asbestos in the vicinity of a point source with an emission of 10 kg per year; source height 8m; Schiphol climatology

Distribution on a road/street scale

This distribution is heavily dependent on traffic intensity and on whether the road lies inside or outside the built-up area. Estimates were made analogous to those of the NOx emission (Van den Hout et al., 1983), using the fact that the number of car kilometres travelled outside the built-up area is twice as great as that inside it. For asbestos, the emission factor is highest inside the built-up area (more frequent braking), so that the outside/inside ratio is less than 2. It was estimated that the emission factor inside the built-up area is twice as large as that outside it. It can be inferred from this that of the total asbestos emission on roads (600 kg per year, table 2.14.), 300 kg per year end up both inside and outside the built-up area (this does not include any possible contribution from the use of asbestos-containing waste as road paving, and re-emission). If it is furthermore assumed that the concentration contributions are roughly proportionate to the emissions, then the following concentration levels are found (table 3.1.):

Table 3.1. Estimated contributions made by road traffic to the asbestos concentrations along roads and streets, in ng.m^{-3}

Busy streets in large towns	*: 0.5 - 1.4*
Quiet streets in large towns	*: 0.2 - 0.3*
Busy streets in villages and small towns	*: 0.3 - 1.1*
Busy motorways, roadside	*: 0.15- 0.5*
Busy motorways, 100 m from the road	*: 0.1 - 0.2*

It can be inferred from these values that traffic can increase the average national and urban levels by 0.2-1.4 ng.m^{-3}, depending on the traffic intensity. The results of measurements in the Netherlands are roughly in line with these figures.

3.3.2. Deposition

Asbestos fibres are removed from the air by Brownian movement, interception and impaction, depending on the aerodynamic diameter of the fibres. The very small fibres behave approximately as molecules and undergo Brownian movement, so that they can coagulate into larger dust particles, which then sediment. Interception occurs with the larger fibres, when the particle is able to align itself with the streamlines in front of an obstruction but is subsequently intercepted by the obstruction. Impaction occurs when a particle cannot align itself with the streamlines because of sluggishness.

To be able to estimate the deposition velocity, the aerodynamic diameter of a fibre must be known. Deworm and Pauwels (1976) concluded that the aerodynamic diameter of a fibre is 3 to 5 times the geometric diameter. Gonda and Khalik (1985) calculated the aerodynamic diameters of fibres (cylindrical and spheroidal form) for parallel or perpendicular flow and when the fibres were randomly orientated with respect to the airflow. Table 3.2. lists factors which, when multiplied by the geometric diameter, give the aerodynamic diameter.

Table 3.2. Multiplication factors for the calculation of the aerodynamic diameters of chrysotile fibres on the basis of the geometric diameters

Factor length/diameter (aspect)ratio	*Fibre = cylinder (random orientation)*	*Fibre = elongated spheroid (random orientation)*
5	*3.0*	*2.4*
10	*3.4*	*2.7*
15	*3.6*	*2.9*
20	*3.7*	*3.0*
25	*3.8*	*3.1*

Table 3.2. shows that, for $5 < l/d < 25$, the aerodynamic diameter is 3 to 4 times the geometric diameter, depending on the fibre approach chosen. Because of the difference in density, the aerodynamic diameter of amosite is 1.16 times that of chrysotile. This factor is 1.14 for crocidolite.

Dry deposition

For areas with local sources, for large towns, industrial zones, middle-sized towns and "background" areas, Lanting and den Boeft (1983) found the following average aspect ratio for chrysotile fibres:

- areas with a local source 40 (range: 17-61)
- large town 35 (range: 14-84)
- road tunnel 23 (range: 17-35)

The median diameters for the various areas are, irrespective of the area, 0.1 μm with a small scatter (a few 0.01 μm). It can be deduced from the average diameter (0.1 μm) and the average aspect ratio (about 30) that chrysotile fibres 0.1 μm in diameter and about 3 μm long are the most common. These fibres have an aerodynamic diameter of 0.3 to 0.4 μm. Table 3.3. gives a few dry deposition velocities which are possibly applicable to asbestos fibres. Table 3.3. shows that there is a large variation in the magnitude of the deposition velocity and the circumstances under which it

was determined. At a mixing height h of about 1000 m and a removal constant $k_d = V_d/h$, the half-life $t_{1/2} = \ln 2/k_d$. For the deposition velocity range of 0.03-0.20 $cm.sec^{-1}$, the half-life is 100 to 600 hours. At a wind speed of 5 $m.sec^{-1}$, asbestos fibres could be transported over a distance of more than 2000 km.

At an annual average concentration of 0.1 ng chrysotile.m^3, taking into account the large spread in the deposition velocities (0.03-0.20 $cm.sec^{-1}$), the annual load in the Netherlands due to dry deposition is estimated at 50 to 250 kg.

Table 3.3. Dry deposition velocities

Particle size (μm)*	*Deposition velocity (cm/sec)*	*Details*	*Reference*
0.1 - 1	*0.03*	*lab. experiments, onto grass surface*	*McMahon and Denison (1979)*
0.1 - 10	*0.05 - 5*	*open air experiments, onto filter paper and glass surface*	*Esmen and Corn (1971)*
0.3 - 0.4	*0.03*	*deduced from deposition velocity versus particle size, for Eucalyptus forest*	*Slinn (1982)*
0.01 - 10	*0.01 - 1*	*theoretical model*	*Sehmel (1980)*

* *type of particles not known*

Wet deposition

A limited number of facts are known about concentrations of asbestos fibres in precipitation. Den Boeft and Lanting (1981) reported that, during a period of much precipitation, the passive loading of filters protected from rain decreases. Passive loading is the result of dry deposition. If it is assumed that the dry deposition is proportional to the concentration in the air, then it must be concluded that rain is an efficient mechanism for removing fibres. This was found to be especially true for chrysotile fibres.

Cunningham and Pontefract (1971) found more than 3×10^7 fibres.l^{-1} in melting snow in Canada. Hesse et al. (1977) found for wet deposition in Chicago 10^5-10^6 fibres per litre of precipitation. The sooner the sampling was begun after it had started to rain, the higher the concentration levels in the precipitation collector, which confirms the above conclusion.

Den Boeft and Lanting (1981) found in precipitation in the vicinity of a local source 5 to 20×10^6 chrysotile fibres per litre of rainwater. The results are comparable to those found by Hesse et al. (1977) for the total

deposition. The above-mentioned results were obtained using a transmission electron microscope (TEM), with which much thinner fibres can be seen than with the scanning electron microscope (SEM). Lahmann (1979), using the SEM, found $< 10^4$ fibres per litre of rainwater in a precipitation collector in Berlin (fibre dimensions $d > 0.1$ and $l > 1$ μm).

Hesse et al. (1977) stated that the wash-out of asbestos fibres is proportional to the concentration in the air. Measurement results (Den Boeft and Lanting, 1981) showed that the concentrations of asbestos fibres in the air, in the area where the deposition samples were taken, were about 50 times higher than the estimated annual average concentrations of asbestos fibres of about 0.1 $ng.m^{-3}$. This gives an annual average deposition level (wet and dry) of 1-4 x 10^5 chrysotile fibres per litre of rainwater. Cunningham and Pontefract (1971) used a conversion factor for water samples of 10^7 chrysotile fibres.μg^{-1}. Conversion factors should be used with the necessary caution, because this factor depends heavily on the length and diameter distributions of the fibre population under consideration.

With an average annual precipitation in the Netherlands of 775 mm, a surface area of 4 x 10^{10} m^2 and a fibre deposition of 1-4 x 10^5 fibres.l^{-1}, the total annual deposition is estimated to be 300-1250 kg. Subtracting from this the dry deposition of 50-250 kg leaves 250-1000 kg per year for the wet deposition.

Re-emission or resuspension

Re-emission or resuspension is the process by which particles are again taken up in the air through the action of the wind or mechanical activity. Since asbestos fibres are relatively inert, they can remain in the environment for an appreciable time. The fibres can begin to participate in a cycle, consisting of the removal through dry and wet deposition of fibres from the air which, perhaps after drying, can again be taken up in the air. The portion reaching the water is withdrawn from the air-soil-air cycle, but can re-enter the air via other routes.

The wind conditions together with the relative humidity and mechanical activity determine how many fibres can end up in the air after they have been released from a matrix. Concerning waste disposal sites and the like, the extent of covering plays an important role.

Baxter et al. (1983) concluded that near sources the concentrations are generally higher when there is little air movement than when there is wind. Apparently, a slight movement of air is sufficient to dislodge fibres from the substratum but is insufficient to bring about dispersion in the atmosphere.
Possibly the increased concentrations of asbestos fibres in the large towns are maintained chiefly by re-emission. An indication of re-emission was obtained at a monitoring station where a wind direction-dependent sampler was used (Den Boeft and Lanting, 1981): elevated concentrations were also observed when the station was upwind of the local source.
Near dumping sites for asbestos(-containing) waste, which were usually situated in areas which would have been "background" without these dumps, the concentrations measured were 10 to 100 times higher than the background concentration levels (Murchio et al., 1979; Harwood and Blaszak, 1974). These concentrations must be due to a combination of emission during the dumping and handling of the waste and re-emission.
Asbestos cement waste was used at several locations in the province of Overijssel for paving sandy roads and yards, etc. When a dry road surface is used intensively, asbestos fibres could possibly be set free from the cement matrix. Den Boeft (1987) measured the concentrations near such a road. He found elevated concentrations in the immediate vicinity of the road under dry conditions. Increased concentrations were not measured when there was more than an average amount of precipitation.

3.4. SUMMARY AND CONCLUSIONS

Asbestos fibres are highly inert and can consequently remain in the environment for an appreciable time.
Despite the fact that most asbestos ends up on and in the soil particularly as a result of the dumping of waste products, the extent of asbestos transport to groundwater and subsequently surface water is limited. Asbestos fibres are readily transported via water and air and they may cover distances of hundreds and thousands of km respectively. The levels in the air are dertermined by both emission and re-emission or resuspension, whereby the emission will contribute (permanently or temporarily) to elevated concentrations especially on a local scale, and the re-emission (through the action of the wind or mechanical activity) will exert a substantial influence on the large-scale concentration levels. Asbestos

fibres are removed from the air by dry and wet deposition, depending on the aerodynamic diameter of the fibres.
The wet and dry depositions are about 250-1000 kg and 50-250 kg per year respectively.

4. MEASUREMENT TECHNIQUES

A variety of analysis techniques are available for the determination of asbestos, which can roughly be divided into techniques for macrosamples (asbestos-containing materials) and those for microsamples (environmental samples). The bulk analysis methods such as infrared spectroscopy and X-ray diffraction do not analyze single fibres but determine the total asbestos content. In the case of the environmental samples, however, individual fibres are detected and, if required, identified using a microscopic technique. Although sample preparation differs for each of the environmental samples, the microscopic techniques used are virtually the same.
The literature consulted has been summarized in section 9.4. and will only be referred to occasionally.

4.1. ANALYSIS TECHNIQUES

4.1.1. Analysis techniques for determination of asbestos in bulk samples

X-ray diffraction (Brantley et al., 1982; Taylor, 1978)
The so-called X-ray powder diffraction method is generally used in practice, the sample consisting of a large number of randomly orientated crystals. It produces a characteristic line spectrum, the intensity of which is a relative measure of the concentration in the sample.
The advantages of X-ray diffraction are that identification is specific for a particular crystalline compound and that it allows quantitative determination of asbestos. The disadvantages are: (a) the method is relatively insensitive (about 2% asbestos by weight) and consequently not suitable for trace analyses; (b) diffraction patterns of fibrous asbestos are almost identical to those of the mother rock, which has a very similar crystal structure. This problem can be overcome by orientating the fibres prior to analysis in an electric or magnetic field, so that a preferred orientation is obtained. However, these preliminary treatments are complicated and require special equipment which is usually not commercially available.

Infrared spectrometry

IR spectrometry is based on the characteristic absorption of infrared radiation by asbestos and has roughly the same application area as X-ray diffraction. However, the qualitative information obtained from the spectra is less unequivocal, which limits the utility of this method.

The advantage of IR spectrometry is that it is rapid and therefore relatively cheap. With Fourier Transform IR, in particular, matrix corrections and automatic data processing are relatively easy. The disadvantage is that, although the mineral chrysotile has a characteristic spectrum, the spectra obtained from the other asbestos types (which all possess an amphibole structure) are not readily distinguishable from each other. Moreover, the risk of interference by other silicates is quite high. Accordingly, the application area is usually limited to asbestos analyses in industrial products with a well-known matrix.

Polarized light microscopy (Van Maaren, 1984; Virta et al., 1982)

This technique identifies asbestos types on the basis of characteristic optical properties such as the index of refraction, behaviour in polarized light, birefringence and dispersion. This method is particularly suitable for rapid identification of asbestos in materials such as asbestos cement or insulation.

Other methods (Benarie, 1983; Surkyn et al., 1983; Jones et al., 1982, 1983)

- Differential thermogravimetry

In differential thermogravimetry, changes in weight are recorded while traversing a given temperature range, whereby temperature and weight are recorded accurately. The method is reasonably specific but very insensitive. The application area is therefore limited to the analysis of industrial asbestos-containing products.

- Light scattering by magnetically orientated fibres (Chatfield, 1982)

Asbestos fibres can exhibit both paramagnetic and ferromagnetic behaviour when they are exposed to a strong magnetic field. Because of the strong preferred orientation, a beam of laser light will be scattered by the fibres in a particular pattern. In this way, the fibre concentration in a

suspension can be determined and the scattering behaviour can give an idea of the fibre diameter distribution. this method has not been standardized.

-Fibre monitor
With the fibre monitor, the fibre concentration in the atmosphere can be measured continuously. The fibres in an air flow are again brought into a preferred orientation followed by measuring the light scattering. The fibre monitor is not completely specific for asbestos but it is suitable for measuring high asbestos concentrations, for example, in process monitoring in the asbestos industry or in exposure rooms for inhalation experiments.

- Selective staining of asbestos fibres
Chrysotile fibres stained with selective fluorescent dyes can be detected with a fluorescence microscope. This method requires many preparatory treatments of the samples.

- Lasar Raman microprobe
Analysis of asbestos using the lasar Raman microprobe is still in the experimental stage and is not yet suitable for general application.

4.1.2. Microscopic measurement techniques

Phase-contrast optical microscopy
Traditionally, phase-contrast microscopy is the most widely used technique for determining asbestos fibres in air samples. This method has been laid down in a number of standard specifications (NNI, 1987; Asbestos International Association and EEC, 1983), which describe in detail the manner of sampling and preparation, counting rules, etc.

- Counting rules
A fibre is defined as a particle with a length/diameter ratio of at least three. Only fibres with a length of over 5 μm and a diameter of less than 3 μm are counted (detailed counting rules have been laid down in the Dutch concept standard NVN 2939 (NNI, 1983) and in Directive 83/477/EEC (EG, 1983).

- Resolution and visibility

The visibility of the fibres is determined by a large number of factors (Rooker et a., 1982; Heidermanns, 1978), including the difference in refractive index between fibre and embedding medium, the quality of the specimen and the resolving power of the microscope. The visibility limit lies usually around 0.3 μm as the minimum fibre diameter, which means that a large proportion of the asbestos fibres sampled are not discernible with a light microscope. In the workplace, near the emission sources, a considerable fraction of the fibres has a diameter of more than 0.3 μm and the fibres can thus be observed, but 95% to 99% of the fibres in the outdoor air are submicroscopic. Light microscopy is therefore not suitable for determining asbestos in ambient air, unless sources are in the immediate vicinity.

Advantages:
- the method has been internationally standardized (ISO and AIA) and periodic comparative checks ensure that its quality is maintained;
- light microscopy is relatively cheap so that the counts can also be performed by small company laboratories;
- the method is the only one which has been validated for comparison with the MAC value.

Disadvantages:
- resolution is limited so that a large number of fibres (also of the fraction which poses a potential risk to health) are not observed;
- identification of single fibres is not always possible;
- the method is not suitable for determining the concentration of asbestos fibres in the ambient air.

It may be expected that the counts will increasingly be automated (Kenny, 1981). This automation will lead to a much greater measuring precision and eventually to a lowering of the analysis cost.

Scanning electron microscopy (SEM)

The scanning electron microscope (SEM) is used for both qualitative and semi-quantitative asbestos analyses. Its resolving power is many times greater than that of the light microscope. The SEM can be fitted with X-ray microanalysis equipment with which fibres can be identified on the basis of their chemical (elemental) composition by X-ray fluorescence.

Advantages:
- specimen preparation is simple so that the sample preserves its original state as far as possible;
- identification by X-ray microanalysis is possible;
- SEM has a very great depth of field.

Disadvantages:
- Unequivocal identification by X-ray microanalysis is not possible when the fibre diameter is less than about 0.5 μm;
- fibres with a diameter of less than 0.1 μm are often not readily observable with sufficient contrast;
- optimum resolution is obtained at high magnifications only;
- application of electron diffraction is not always possible.

Here, too, automatic image-processing will be introduced at a great pace. Advanced preparation techniques will further improve the image quality.

Transmission electron microscopy (TEM)

In TEM, unlike SEM, an electron beam is used as the image-forming medium. TEM gives a much higher resolution than SEM and this is already achieved at relatively low magnifications. When used in conjunction with X-ray microanalysis (RMA), elemental fibres with a diameter of as little as 0.02 μm can still be identified. TEM is suitable for electron diffraction on single particles, with which in principle the same crystal parameters can be determined as with X-ray microanalysis, albeit with a larger variation in the calculated d values. TEM has thus a greater analytical capability for the examination of asbestos than REM and is therefore more suitable for trace analyses in environmental samples.

Advantages:
- resolution is very high so that even the smallest fibres can be seen;
- when used in conjunction with X-ray microanalysis (RMA), very small particles can be identified;
- electron diffraction on a microscale is possible. This technique is applied especially to complex mixtures of minerals which differ little in their elemental composition (for example, asbestos in talc);
- there is a concept EEC standard specification for analysis of asbestos by TEM (Burdett, 1984);
- accurate fibre size distributions can be determined.

Disadvantages:
- preparation of the sample for TEM is more complicated and consequently more expensive than for SEM;
- the specimens are small so that a great deal of attention must be paid to the sampling, in order that the material analyzed is as representative of the total sample as possible.

Scanning transmission electron microscopy (STEM) in conjunction with automated image processing will make possible a fully automated qualitative and quantitative analysis. As a result of a reduction in the analysis cost, TEM will also become applicable to the analysis of occupational samples. This requires further improvement of the preparation technique.

Energy dispersive X-ray microanalysis

With energy dispersive X-ray microanalysis, elements of atomic number 6 (Carbon) and higher can be detected. A wavelength dispersive measurement technique can in principle also be used with which a higher resolution is obtained. However, this method is time-consuming so that the much quicker energy dispersive procedure is usually preferred in practice.

Selected area electron diffraction (SAED)

It is possible to identify single particles in the TEM by means of electron diffraction. The d values can be determined from the diffractogram, albeit with lower precision than is possible with X-ray diffraction. Identification by SAED is reliable but time-consuming and requires specialist knowledge.

4.1.3. Quantitative analysis

One disadvantage of any quantitative microscopic analysis is that only a fraction of the sample can be examined. It is therefore highly important that the specimen is homogeneous. The accuracy of the analysis increases as a larger fraction of the sample is examined. With electron microscopy in particular, however, this is labour-intensive and expensive, so that a compromise has to be found between the cost and the desired accuracy of the analysis. The density of the specimens should be chosen in such a way that the particles do not overlap. A known area is scanned for fibres which are then identified by RMA or, if required, SAED. The length and diameter of the fibres are also determined. This size distribution is important in studies of dose-response relationships.

4.2. SAMPLING OF AIR

4.2.1. Sampling for light microscopy

A known volume of air is passed through a cellulose ester membrane filter with a pore size of 0.8 or 1.2 μm at a flow rate of 1-2 dm^3 per minute. The filter diameter chosen is usually 25 or 37 mm. A pump with an electronically maintained constant flow rate should preferably be used, although a pump with a critical opening is a useful alternative for fixed sampling points. The sampling time can vary between 0.3 and 8 hours,

depending on the expected concentration. With high concentrations, a number of short-period samplings are carried out in order to increase the reliability of the measurement. The filter holder should preferably be made of metal to suppress the formation of static electricity. The filter support should be such that the suction rate is the same at all points to prevent inhomogeneous distribution of fibres over the filters, which leads to wide variations in the microscopic count.
In flue gas or ventilation ducts, samples are preferably taken isokinetically. Here, the suction openings should not be too small.

4.2.2. Sampling for electron microscopy

Since electron microscopy is usually applied to trace analyses, larger volumes of air are sampled than for light microscopy (100-1000 m^3). Concentration of the samples by ashing is then necessary.
SEM samples can be collected directly on Nuclepore filters. The resistance of these filters is high, however, and increases with the degree of loading so that only high volume pumps can be used. The filters are gold coated by vacuum evaporation beforehand. This suppresses static charging, protects the filter material during ashing in an oxygen plasma and gives a high contrast in the SEM (König and Seger, 1983).

4.3. PREPARATION TECHNIQUES FOR ELECTRON MICROSCOPY

The different types of environmental samples are treated identically except for the preparatory stage. The aim is always to release the asbestos fibres as selectively as possible from the matrix, followed by concentration and preparation.
When a membrane filter is prepared for analysis, it is assumed that the particles are distributed evenly on the filter (Poisson distribution). This requires very careful filtration. The filter is treated with acetone vapour followed by "etching" in an oxygen plasma for 10 minutes. After drying, a carbon film is deposited on it by vacuum deposition, a small piece is cut out of the filter and mounted on a TEM specimen grid. The filter material is subsequently dissolved in acetone so that the carbon film with asbestos particles is left behind on the TEM grid.

Water samples

The water is filtered directly through a membrane filter. Clogging of the filter, for example, by the formation of an iron hydroxide precipitate can be remedied by rinsing the filter with a solution of oxalic acid. The samples can be further concentrated by ashing, where required.

Air samples

The concentration of asbestos fibres in the workplace is often relatively high. In most cases, therefore, a concentration step is not required, and the samples and the filter can be prepared directly for analysis.
Asbestos fibres are present in trace concentrations in the ambient air, so that one pre-concentration procedure is required. The sampled filter is ashed at low temperature in an oxygen plasma. The asbestos residue is dispersed in water by ultrasonification and refiltered through a membrane filter.

- Lung tissue

Lung tissue is dissolved in an enzyme or an alkaline solution or ashed in an oxygen plasma. The ash residue is then usually treated with a hydrochloric acid solution to release the fibres from their often iron-rich coat, among other things.

4.4. SUMMARY AND CONCLUSIONS

Table 4.1. summarizes the various analytical techniques, their application area and the approximate analysis cost per sample.
X-ray diffraction used in conjunction with polarizing microscopy is a reliable and well-documented technique for determination of asbestos in most types of bulk samples. Transmission electron microscopy (TEM) in conjunction with X-ray microanalysis (RMA) or electron diffraction (SAED) is the most appropriate technique for trace analysis in environmental samples.
For the time being, standardized microscopic analysis methods are still indispensable for determination of asbestos in environmental samples.
The application of automatic image-processing and automatic microanalysis will ensure that in the near future electron microscopy will increasingly be used for the analysis of environmental samples. The preparation techniques still require further improvement. A number of new techniques

look promising, for example, light scattering by magnetically orientated fibres. However, it will still take several years before these techniques are available in the form of standardized measurement methods.

Table 4.1. A summary chart of the principal analysis techniques for asbestos

Sample type	*Asbestos concentration*	*IR spectrometry*	*X-ray diffraction*	*LM phaco*	*LM polarization*	*SEM + RMA*	*TEM + RMA*	*TEM + SAED*	*Remarks*
Bulk samples									
insulating material	*0.1-100 % by wt*	* ***	* ***		* **	*			
asbestos cement products	*10-30 % by wt*	* ***	* ***			*			
Trace analyses									
Talc powder etc.	*0.001-10 % by wt*		* ***	**	*		* **	*	*standardization in preparation*
air samples workplace	*50-50,000 ng*			***	*	**	**		*LM phaco stand. EEC method*
air samples ambient air	*1-500 ng*						* ***	*	*concept EEC standard for TEM/RMA*
lung tissue	*1-5000 ng*			*			* ***	*	
water	*1-5000 ng*			**			* ***	*	
soil	*0.01-5 % by wt*				**	**	**	*	
Approx. analysis cost per sample		*F200*	*f500*	*f300*	*f500*	*f800*	*f2000*	*f3000*	
Required level of knowledge		*M*	*H/U*	*M*	*H*	*H*	*H/U*	*U*	

* = qualitative; ** = semiquantitative; *** = quantitative;
M = MBO, intermediate vocational education; H = HBO, higher vocational education; U = university

5. CONCENTRATIONS IN THE ENVIRONMENT AND EXPOSURE LEVELS

An extensive literature has been published on exposure to asbestos. However, the results of the various studies cannot readily be compared because the authors have used both different analysis methods and different units of measurement, and some have focused on certain fibre lengths and diameters, which others have not. In industrial hygiene, it is customary to express the asbestos concentration in numbers of fibres, longer than 5 μm, per m^3, as determined with a light microscope (chapter 4). On the other hand, the concentration in non-occupational situations is usually expressed in $ng.m^{-3}$. There is no conversion factor between the two units of measurement because this factor depends, among other things, on the environment (asbestos variety, fibre size distribution) and the sampling and analysis techniques used (chapter 4). Various conversion factors have been reported in the literature (Levine and Suta, 1979; Spurney et al., 1979; National Research Council, 1984). Broadly, 1 $nm.m^{-3}$ corresponds to 2,000-40,000 $fibres.m^{-3}$.

Results of ambient air measurements (Den Boeft and Lanting, 1981) showed that, irrespective of the observation site, the chrysotile fibre diameter lies within a narrow range around the median value of 0.1 μm (the diameter of elemental chrysotile fibres is 0.03 μm). The contribution of these small dimensions (mainly diameter) to the mass concentration can be illustrated as follows: one optically visible fibre with a diameter of 1.0 μm and a length of 5.0 μm has the same mass as 4.5×10^4 elemental fibres of chrysotile with a length of 0.15 μm. Furthermore, it was found that only 10% of the fibres longer than 5 μm observed with the transmission electron microscope (TEM) can be detected with the light microscopic (LM) analysis methods. To link up as far as possible with the literature, the asbestos concentrations in the work environment (subsection 5.5.1.) have been expressed in number of fibres per m^3, the other concentrations in $ng.m^{-3}$.

5.1. BACKGROUND CONCENTRATIONS

Because of their thermal and chemical properties (chapter 1), asbestos fibres can remain in the environment for long periods of time and be transported over considerable distances via both air and water. As far as is known, no measurements have been made at locations far removed from asbestos sources, for example, oceans. Den Boeft and Lanting (1981)

reported a few asbestos concentrations, measured in rural and "background" areas in the United States and at 2 locations in Europe (table 5.1.).

Table 5.1. Asbestos concentrations in a few rural and "background" areas

Type of area	*Asbestos concentration*		*Analysis method*
	(ng/m³) range	*(fibres/m³) range*	
"Background" area			*TEM*
California (USA)	*0.02-0.15*	*-*	*d<0.5 μm; l<2.5 μm*
Rural areas, UK	*0.1 -1*	*-*	*TEM*
Rural areas, FRG	*0.11-0.23*	*110-230*	*TEM*
"Background" area, FRG	*0.03-0.07*	*30-70*	*d=0.5 μm; l=2 μm*

Den Boeft and Lanting (1981) made measurements at several locations in the Netherlands which were dozens of km removed from (potential) sources. The concentrations of chrysotile fibres measured at these stations were 10^2-10^3 fibres.m^{-3} ($\leq$ 0.1 ng.m^{-3}). It should be noted here that this value is close to the detection level of the analytical method employed.

5.2. OCCURRENCE IN THE SOIL

Nothing is known about the occurrence of asbestos fibres in the soil.

5.3. OCCURRENCE IN SURFACE WATER

Asbestos fibres can be present in both ground and surface waters, depending on the geological situation and the contamination via discharges and manufactured products. As far as is known, systematic measurements of asbestos fibre concentrations in the Dutch surface water have not been made. Such measurements, however, have been made at several locations in the United States and Canada (table 5.2.).

Table 5.2. Asbestos concentrations in surface water in the United States and Canada by the TEM analysis method

Location	*Concentration (fibres/l)*	*Reference*
Ottawa river (Canada)	*9.5×10^6*	*Cunningham and Pontrefact (1971)*
Ontario (Canada)	*0.1-3.9×10^6*	*Kay (1973)*
Lake Michigan (US)	*1.8×10^6 (4.2×10^5-4.2×10^6)*	*McMillan et al. (1977)*

Levels of up to 2×10^9 asbestos fibres.l^{-1} were encountered in a few cases (Oliver and Murr, 1977), where the surface water was contaminated with

asbestos fibres from asbestos-bearing rock with which the water was in contact.

5.4. OCCURRENCE IN AIR

5.4.1. Indoor air

- Exposure in the work environment

There is a risk of occupational exposure during the handling of asbestos cement products on site (sawing, grinding). Riediger (1981) reported 0.06-0.2x10^6 fibres.m^{-3} (chrysotile asbestos) during the cutting to size of the materials. Rödelsperger et al. (1980) found an average fibre concentration of 20x10^6 fibres.m^{-3} near the head of the operator of a slitting machine. Higher concentrations are produced when these activities are carried out in enclosed areas, especially during the use of a grinding wheel. Woitowitz and Rödelsperger (1981) found on average 50x10^6 fibres.m^{-3}, resulting in a time-weighted average (TWA) of about 5x10^6 fibres.m^{-3}.

Certain brake linings contain 10-50% chrysotile asbestos by weight. Exposure occurs especially when the brake drum is blown out with compressed air, in the absence of an exhaust system. Jahn et al. (1985) found values of about 6x10^6 fibres.m^{-3}, with a maximum of 20x10^6, for the peak concentrations. Roberts (1979, 1980) reported a peak concentration of 0.33x10^6 fibres.m^{-3} during cleaning of the drum by air, and 2.6x10^6 fibres.m^{-3} during wet cleaning. Riediger (1984) found 0.6-0.9x10^6 fibres.m^{-3} during the grinding of the brake lining; Jahn et al. (1985) found up to 0.4x10^6 fibres.m^{-3}. The average concentrations during the entire procedure were between 0.04 and 0.3x10^6 fibres.m^{-3} (Roberts, 1979, 1980; Nicholson et al., 1982; Jahn et al., 1985).

The use of asbestos-based fillers for the finishing of walls can constitute a significant source of environmental contamination.

The highest concentrations occur during mixing, grinding and sweeping (Fishbein et al., 1979); Verma and Middleton (1980) reported an average concentration for all operations of 6-18x10^6 fibres.m^{-3} (range 0.3-25x10^6 fibres.m^{-3}). Although the spraying of asbestos is now prohibited, sprayed asbestos layers are often still present in, for example, factories, warehouses and offices. As a result of mechanical damage and ageing, the asbestos fibres can be set free and dispersed. A study at 29 locations found concentrations ranging from <0.001x10^6 to 0.6x10^6 fibres.m^{-3}

(Tempelman et al., 1985). It here generally involves amosite fibres. During work on or in the vicinity of sprayed insulation (e.g. the installation of new cables), Arhelger et al. (1984) found concentrations of up to $20x10^6$ fibres.m^{-3}, with a geometric mean of $0.08\text{-}0.2x10^6$ fibres.m^{-3}, depending on the type of work carried out.

Relatively little attention has been paid to exposure of workers during the demolition of buildings or the removal of sprayed asbestos layers, for which Arhelger et al. (1984) found a peak concentration of $200x10^6$ fibres.m^{-3} (crocidolite); the TWA was about $15x10^6$ fibres.m^{-3}. Marfels et al. (1984) found lower concentrations during the removal of a sprayed asbestos layer, viz., between 0.3 and $0.5x10^6$ fibres.m^{-3}.

Breman (1984) monitored the air concentrations of crocidolite asbestos over time during the removal of the thermal insulation of a turbine in a screened-off area. Peak concentrations of $> 25x10^6$ fibres.m^{-3} were found inside this area; the concentrations outside were $< 0.01\text{-}0.8x10^6$ fibres.m^{-3}.

Since the introduction of the asbestos regulations, the MAC values in occupational situations are not exceeded in Europe. In the secondary sector, too, equipment designed to operate below the MAC value is now available.

- Non-occupational exposure

Although asbestos-free alternatives are now being used, there still exist a large number of asbestos-containing products. Asbestos has been used, among other things, in electric appliances (toasters, flat-irons, hairdriers, etc.), floor coverings, ironing board pads, asbestos plates (e.g. table mats), water pipe laggings, and chimney and stove caulking compounds.

Quantitative information about the effect of this asbestos on the air concentration inside dwellings is not available. It is generally assumed that this concentration is roughly similar to the concentration in the outdoor air, the latter being on average $< 0.1\text{-}0.3$ ng.m^{-3} in the Netherlands (see subsection 5.4.2.). Sprayed asbestos materials have been used in public buildings such as schools, theatres, shopping centres, gymnasiums and swimming baths. The concentrations measured in the Netherlands in buildings in which sprayed asbestos layers are present varied between < 1 and 6,000 ng.m^{-3} (Tempelman et al., 1985). Sebastien et al. (1982) found concentrations of up to 170 ng.m^{-3} caused by a chrysotile-containing floor covering.

5.4.2. Outdoor air

Asbestos concentrations in the ambient air have been measured at many locations in Europe and North America. It usually involved spot checks with brief sampling periods (several hours to days). The comparability of the results, which showed wide variations, is hampered by differences in such factors as sampling method, sampling duration, sample preparation technique, analysis method, fibre definition and processing method used for the analysis results. The ISO is aiming to achieve standardization of measurement methodology and data processing at an international level. Concentration measurements were made in the Netherlands between 1978 and 1980. The concentrations measured were monthly averages based on weekly samples. Air samples were taken during at least three consecutive months from each station and analyzed by TEM. The results for chrysotile are shown in table 5.3.

Table 5.3. Monthly average fibre and mass concentrations of chrysotile asbest, measured at various locations in the Netherlands (Den Boeft and Lanting, 1981)

Sampling station	*Fibre concentration (fibres/m3)*		*Mass concentration (ng/m3)*	
	average	*range*	*average*	*range*
Near sources:				
Goor (400 m from source)	*40,200*	*5,500-80,000*	*6*	*0.4-15.5 (316)****
	*6,400**	*200-13,400**	*2**	*<0.1-7.1**
Harderwijk (600 m from source)	*1,600*	*400- 2,800*	*0.3*	*<0.1-0.8*
Harderwijk (200 m from source)	*37,000*	*1,300-50,000*	*4*	*1.2-6,7 (105,171)****
Delft (100 m from source)	*18,200*	*10,500-24,600*	*2*	*1.0-2.8*
Bergh, motorway	*5,200*	*1,500-10,700*	*1*	*<0.1-1.5*
*IJtunnel***	*59,100*	*38,200-80,800*	*9*	*7.3-13.0*
In large towns:				
Rotterdam	*4,700*	*<200-11,000*	*0.3*	*<0.1-1.0*
Amsterdam North	*7,800*	*1,300-22,700*	*0.8*	*<0.1-2.9*
Amsterdam Centre	*4,400*	*600- 8,300*	*0.3*	*<0.1-0.5*
Amsterdam Geuzenveld	*2,300*	*800- 6,200*	*0.3*	*<0.1-0.7*
In middle-sized towns and "background" areas:				
Delft (Zuidpolder)	*3,600*	*1,200- 9,000*	*0.3*	*<0.1-0.8*
Nieuw Namen	*1,800*	*300- 3,600*	*0.1*	*<0.1-0.2*
Sas van Gent	*1,100*	*300- 1,800*	*0.1*	*<0.1-0.1*
Vlissingen	*2,600*	*700- 5,500*	*0.2*	*<0.1-0.4*
Nieuwdorp	*1,100*	*300- 1,600*	*0.1*	*<0.1-0.4*
Groningen	*1,750*	*900- 3,200*	*<0.1*	
Usselo	*880*	*400- 1,500*	*<0.1*	

** crocidolite ** daily averages *** peak*

In 1979/1980, amphibole asbestos fibres (crocidolite) were found in measurable amounts at Goor only. The fibre concentrations were about 7 times lower than those of chrysotile.

The monthly average concentrations were determined at two locations during one year or longer (Rotterdam and Delft Zuidpolder). The average (approximately annual average) was about 4700 chrysotile fibres.m^{-3}, which is equivalent to a mass concentration of 0.3 ng.m^{-3}. This concentration is in line with the concentrations measured in Amsterdam during a brief period. The annual average mass concentration in the large towns was about 0.3 ng.m^{-3}. Assuming a background level of less than 0.1 ng.m^{-3}, then the national annual average concentration of chrysotile fibres is estimated to be 0.1 ng.m^{-3}.

The frequency of occurrence of a particular length/diameter class can be gleaned from figures 5.1. a and b. The longest fibres, with an average aspect ratio of 40 (fig. 5.1.a), were found in the vicinity of an asbestos-processing factory. Figure 5.1.b shows the chrysotile fibre size distribution in a large town. The average aspect ratio was 35. Traffic measurements in the IJtunnel showed that the average aspect ratio for traffic was 23.

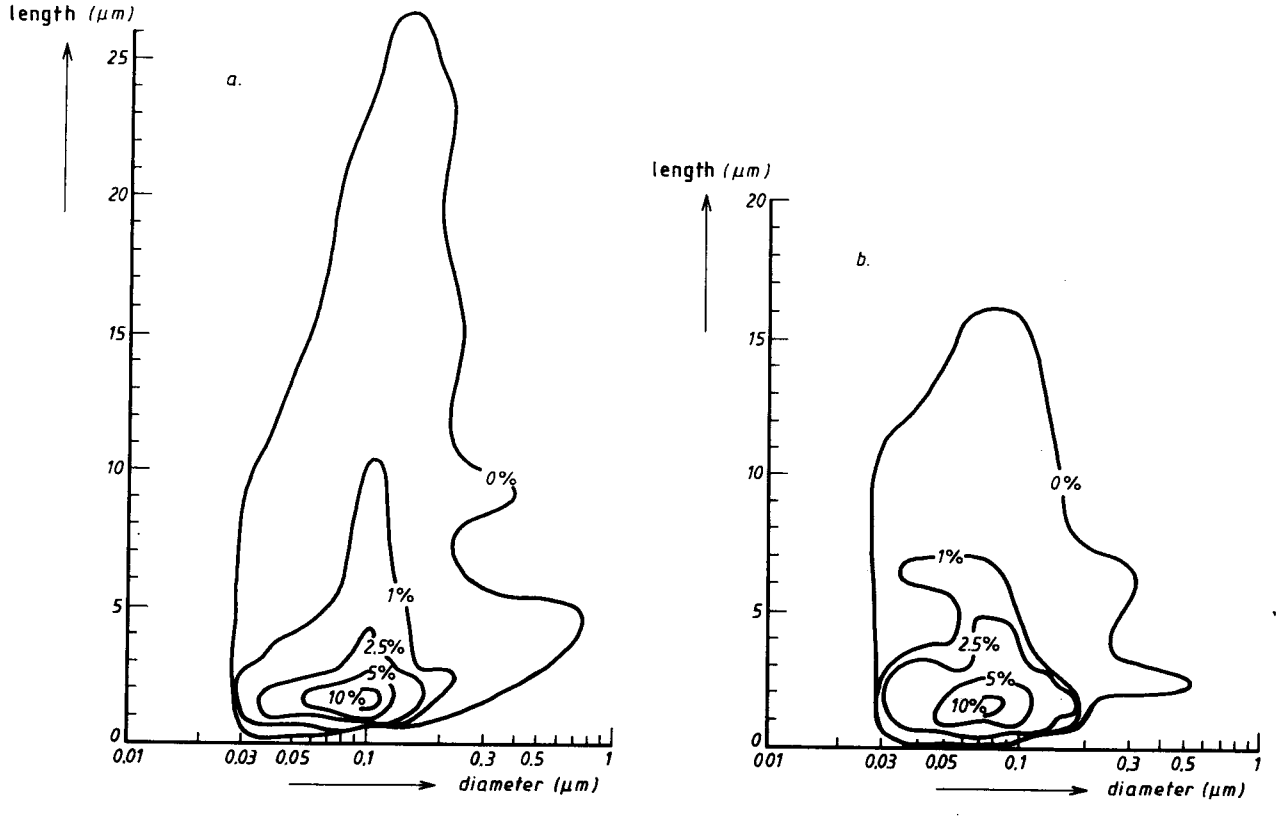

Figure 5.1. Chrysotile fibre size distribution in the vicinity of a source (a) and in a large town (b)

In addition to asbestos fibres, a uniform background level of 10^4 fibres of various types per m^3 was observed.
In general, no link was found between the asbestos concentration (number of fibres/mass) and the concentration of suspended particulates.

5.5. OCCURRENCE IN FOOD AND BEVERAGES

5.5.1. Food and beverages

It was reported in CCRX (1984) that systematic investigation of the occurrence of asbestos in foodstuffs is not being carried out in the Netherlands. The Contaminants booklet (Staarink and Hakkenbrak, 1987) mentions several potential sources of asbestos in the food industry, but information about the actual occurrence of asbestos in food and beverages does not appear to be available.
A review by Rowe (1983) sought to provide more information about the relative importance of food and beverages in the total asbestos intake. It, too, stated that information on this subject is very scarce. It is tentatively concluded that the oral intake of asbestos from food and beverages as well as medicines can be considerable compared with that via drinking water. The explanations offered for the occurrence of asbestos are:

- the filtration of liquid foods and beverages through asbestos filters; this application is not permitted in the Netherlands.
- the presence of tremolite in talc, wich is used as an industrial powder, a filler in medicinal tablets and capsules, and for the treatment of rice and chewing gum.

Rowe (1983), after consultation with FDA experts, made the conjecture that many, if not most, foodstuffs are to some degree contaminated with asbestos.
Rowe (1983) presented an overview based on very limited numbers of measurements, a proportion of which had already been reported in the IARC - Monograph (1979) with data from 1971 and 1973 (table 5.4.).

Table 5.4. Asbestos contents in various beverages, measured by electron microscopy

Product	*Asbestos content (10^6 fibres per litre)*
Beer	*1.1 - 6.6*
Sherry	*2 - 2.6*
Port	*2.1*
Vermouth	*1.8 -11.7*
"Soft drinks"	*1.7 -12.2*

In talc-treated rice, 0.1-3.7x10^{12} fibres per kg were found.
According to Staarink and Hakkenbrak (1982; 1985), the use of talc is permitted in the Netherlands as an anti-hygroscopic agent in common salt (1%), among other products; in Belgium in, for example, table salt (1%), rice (1%) and chewing gum (2%). Similar limits for talc are in force in other countries.
As reported by one large Dutch rice producer, talc (as a polishing agent!) is not used, at least by his company, because of the potential presence of unwanted contaminants. Scheuermann (1979) reported data on beer samples filtered with asbestos filters. These values were appreciably lower: 100-10,000 fibres per litre (also determined by electron microscopy).

5.5.2. Drinking water

Drinking water can contain asbestos fibres derived from the source as well as from the pipe system.
Elzenga et al. (1974) performed analyses on Dutch drinking water from water distribution systems with asbestos cement pipes. The samples of drinking water, which had been prepared from groundwater, were taken in 1972 and analyzed by scanning electron microscopy. The concentrations measured ranged from 6x10^4 to 24x10^4 fibres per litre of water. Actually, the measurements involved two water conduits only, each with two measurement points (mains and tap). According to Commins (1984), the asbestos fibre concentration in drinking water is about 0.2-2.0x10^6 fibres per litre in most countries.
Millette et al. (1980) analyzed samples of drinking water from some 400 different locations in the US: about 11% contained more than 10^6 fibres per litre. Concentrations of more than 10^7 fibres per litre are not uncommon in Canada and the US (Oliver et al., 1977; Toft et al., 1981). Commins (1984) and Meijer (1982) concluded that asbestos cement does not corrode in

situations where the distributed water does not contain aggressive CO_2. The release of fibres is then not measurable or extremely small.

5.6. EXPOSURE LEVELS

Man is exposed to asbestos through ingestion and inhalation.
Rowe (1983) calculated the ingested asbestos exposure resulting from a supposed daily consumption of 360 ml beer, 84 g rice and 3 tablets (0.9 g) of aspirin (!). The calculated exposure was $0.03\text{-}1.14 \times 10^{14}$ fibres per year, almost entirely derived from rice. When rice not treated with talc was consumed, the annual intake was 2.35×10^{9} fibres, from beer and (intensive) aspirin use. Based on a content of 10^{5} fibres per litre, the annual intake via drinking water is 7.3×10^{10} fibres (Rowe, 1983). In view of these limited and, moreover, older research data, a reliable estimate of the total oral intake cannot be made.
As regards the inhalatory exposure to asbestos, the number of respirable fibres is important, the upper limits being a fibre length of 200 μm and a fibre diameter of 3 μm. In the calculation it has been assumed that an individual inhales on average 12 m^3 of air per day, of which 75% is indoor air and 25% outdoor air. For people living in the immediate vicinity of sources, a 24-hour exposure to the outdoor concentration has been assumed. The estimated daily amount of asbestos inhaled by the Dutch population is given in table 5.5.

Table 5.5. Rough estimate of the daily amount of asbestos inhaled per person, excl. occupational exposure

Residential area	*Daily dose (number of fibres)*
Rural areas, middle-sized towns	1.2×10^3 - 12×10^3
Large towns, industrial areas	4×10^3 - 4×10^4
Immediate vicinity of sources	3.1×10^4 - 3.1×10^5

In addition to the difference in the number of inhaled fibres, the fibre dimensions will vary from one residential area to another. As previously mentioned, only a small variation in the (chrysotile) fibre diameter has been observed (0.1 μm), whereas the fibre length differs per type of area. The longest fibres are found near asbestos-processing industries (subsection 5.4.2.; figure 5.1.), i.e. in those areas where the population is also most exposed.

5.7. SUMMARY AND CONCLUSIONS

As far as is possible, the asbestos concentrations and contents observed in the various environmental compartments are summarized in table 5.6. No data are available on the levels in food products for the Dutch situation. Exposure via the air is highest in the immediate vicinity of sources, where, for the assessment of the health risk, the most important fibre lengths are encountered. The daily dose of inhaled fibres per individual in the immediate vicinity of sources is about $3x10^4$-$3x10^5$ fibres; it is a factor of about 30 lower in rural areas and middle-sized towns.

Table 5.6. Summary of asbestos concentrations and contents in various environmental compartments in the Netherlands, excluding the workplace

Uptake route	*Fibre concentration (fibres/m3)*	*Mass concentration (ng/m3)*
Soil	?	?
Surface water	?	?
Air		
outdoor - rural	10^2-10^3	≤ 0.1
- towns	10^3-10^4	< 0.1- 5
- near sources	10^4-10^5	5 - 300
indoor - living area	10^2-10^3	< 0.1- 0.3
- public buildings with sprayed asbestos		< 1 -6000
- factories with sprayed asbestos	< 10^3-$0.6x10^6$	
Food	?	?
Drinking water	10^5 fibres.l^{-1}	

6. EFFECTS

This chapter contains a summary of a comprehensive background report on the effects of asbestos (Montizaan and Van der Heijden, 1989).

6.1. CHEMOBIOKINETICS AND METABOLISM

6.1.1. Ingestion

There is considerable controversy about whether asbestos fibres are able to cross the gastrointestinal wall after ingestion. Rat experiments have shown that the major part of ingested asbestos is excreted into the faeces within 48 hours (Bolton and Davis, 1976). It is possible, however, that a small fraction penetrates into the gastrointestinal wall, crosses it and subsequently reaches the bloodstream and various other tissues and organs. However, the results of experiments with rats and baboons, investigating this passage of fibres across the intestinal wall, are difficult to evaluate: there are several possibilities of confounding contamination of tissues with asbestos, and the available analytical techniques are moreover not very sensitive. Nevertheless, the observed time-dependent increase in the asbestos concentration in the portal blood of rats up till 7 hours after asbestos ingestion demonstrates that fibres can indeed cross the gastrointestinal wall (Weinzweig and Richards, 1983).

Tissues outside the gastrointestinal tract in which asbestos fibres have been observed are liver, lungs, kidney cortex, spleen, omentum, heart, brain, pancreas and lymph nodes (Bolton et al., 1982; Patel-Mandlik and Millette, 1980; Kaczenski and Hallenbeck, 1984; Cunningham and Pontefract, 1973). There appears to be no preference for one particular type of tissue although there are some indications that fibres are gradually redistributed from the tissues towards subserosal foci and lymph nodes. Chrysotile fibres can be partly dissolved in the gastric juice. In the tissues, chrysotile may be similarly broken down, or fragmented into thin fibrils. In contrast, amphibole fibres are fairly resistant to degradation in the body. The proportion of ingested fibres detectable in the tissues was generally low. In three independent rat studies, the maximum amount of fibres recovered per gram tissue was 10^{-11} to 10^{-10} times smaller than the cumulative ingested amount of fibres per gram of body weight (Bolton et al., 1982; Cunningham et al., 1977; Gross et al., 1974). The amount of ingested fibres

which could be recovered from rat lymph was likewise very small (Sebastien et al., 1980). The average length of fibres found in tissues was not consistently different from that of the ingested fibres.
In humans, the absorption of ingested fibres by the gastrointestinal tract was demonstrated by quantitative analysis of fibres in the urine. The urinary amphibole fibre concentration directly reflected the intake with drinking water by volunteers switching from a high to a low amphibole intake. The maximum urinary excretion of fibres, however, was only 0.1% of total intake (Cook and Ohlson, 1979). Cunningham and Pontefract (1973) analyzed the spleen, brain and peritoneum of three individuals with no history of occupational exposure to asbestos. Although chrysotile fibres were found (in concentrations ranging from 0 to 9.2×10^5 fibres per gram tissue), these cannot be related to exposure.

6.1.2. Inhalation

The mechanisms of deposition in the respiratory system which are relevant to inhaled asbestos fibres are interception, which mainly depends on fibre length, and settlement under gravity, which is dependent on the mean aerodynamic (=equivalent) diameter of the fibres (Dae) but relatively independent of fibre length. For straight fibres, the Dae is approximately 3-4 times larger than the actual diameter (Gross, 1981). The upper limit of the respirability of fibres is a Dae of about 10 μm, which corresponds with an actual diameter of about 3 μm for amphiboles, and a fibre length of 200 μm (Lee, 1985).
Particles with a large Dae and/or long fibre length, and particles with a very small Dae (<0.1 μm) are deposited preferentially in the nasopharynx; particles with a Dae of more than 2 μm are mainly deposited in the trachea and bronchi. The particles are relatively rapidly (hours) cleared from these parts of the respiratory system via the ciliated epithelium and transported to the gastrointestinal tract. A large part of the particles with a Dae of between 0.1 and 0.2 μm will penetrate to the deeper - alveolar - region of the lung, which is not lined by ciliated epithelium. Clearance from this part of the lung can take months to years (Raabe, 1984; Lippmann et al., 1980).
Most fibres up to 5 μm long entering the alveolar regions of the lungs are rapidly phagocytized by pulmonary macrophages, but free fibres may also migrate into cells of the epithelium, interstitium, or endothelium of

capillaries. In vitro studies indicated that fibres longer than 5 μm are not always phagocytized completely, with part of the fibres remaining uncovered (Beck and Tilkes, 1980). Only a small proportion of particle-containing macrophages will be transported to the ciliated airways; most macrophages, as well as the free fibres, migrate slowly towards the periphery of the lungs and the pleura, where the asbestos fibres are finally retained. Some fibres, especially the longer ones (> 5-10 μm long), are coated here and form inert asbestos bodies, but many uncoated fibres can also be found in lung tissue. Both rat studies and observations in humans suggest that amphibole fibres accumulate to a greater extent in lung tissue than chrysotile fibres (Wagner et al., 1974; Sebastien et al., 1977). Chrysotile fibres may be partly dissolved, but amphibole fibres are not. Chrysotile may also split into thin fibrils, which are not readily observed.

Studies with rats and dogs have shown that a large part (70-75%) of the asbestos deposited in the lungs is excreted in the faeces. The faecal excretion of inhaled asbestos has a rapid phase, corresponding with the rapid clearance from the lungs via the ciliated epithelium into the gastrointestinal tract, and a slow phase, which probably corresponds with a gradual clearance from the alveolar regions of the lungs (Evans et al., 1973; Morgan et al., 1978; Griffis et al., 1983). The faecal excretion of asbestos by humans also reflects inhalatory exposure (Cunningham et al., 1976). Data on urinary excretion after inhalation of asbestos are not available.

6.2. EFFECTS ON ANIMALS

6.2.1. Oral studies

There are no indications that asbestos causes serious effects in rats after either short-term or long-term ingestion (Meek and Grasso, 1983; Bolton et al., 1982). The only observed noncarcinogenic effect was slight damage to the gastrointestinal mucosa (Jacobs et al., 1978; Amacher et al., 1974, 1975; Epstein and Varnes, 1978).

Of the available oral carcinogenesis studies with asbestos, many did not meet the currently accepted standards for such studies. In the studies which were considered adequate, only a few statistically significant effects were found, in F344 rats and in Syrian hamsters. Dietary exposure

of F344 rats to 1% amosite for life produced an increased incidence of C-cell carcinomas of the thyroid gland and of mononuclear leukaemias, but in males only. The incidence of gastrointestinal tumours was not increased. The tumour types mentioned often occur in this rat strain (McConnell et al., 1983b). An increased incidence of benign neoplasms of the colon was observed in F344 rats given 1% chrysotile with medium-long fibres in the diet for life. However, in another study with the same strain of rats, 10% of the same asbestos variety in the feed did not cause any increase in benign or malignant tumours of the colon after lifetime ingestion (Donham et al., 1980); besides, the reported increase in benign neoplasms was only observed in males, and was only significant when compared with pooled control data from various studies but not when compared with the parallel controls (NTP, 1985). One per cent chrysotile with short fibres and 1% tremolite in the diet of F344 rats did not produce any increased tumour incidence after lifetime ingestion (McConnell et al., 1983b; NTP, 1985).
In Syrian hamsters, 1% chrysotile in the feed caused an increased incidence of adrenal cortical adenomas, but in males only, and no increased incidence of gastrointestinal tumours was observed (McConnell et al., 1983a).
Occasionally reported peritoneal mesotheliomas may be indicative of a carcinogenic effect, since this is a very rare type of tumour which has been associated with asbestos in intraperitoneal animal studies. However, the observed mesotheliomas could also have been caused by inhalation of the asbestos fibres present in the feed. Also, occasional cases are not considered to be evidence of carcinogenicity.
Treatment of rats and hamsters with known animal carcinogens combined with asbestos feeding did not suggest that asbestos is a promotor or cocarcinogen at oral exposure (McConnell et al., 1983a,b; NTP, 1985; Ward et al., 1980).

6.2.2. Inhalation/intratracheal studies

Experiments with rats, mice, hamsters, guinea pigs and rabbits have furnished sufficient evidence that all asbestos varieties are carcinogenic in animals after inhalation (ARC, 1977). The types of tumours most often associated with inhalatory exposure to asbestos are adenomas, adenocarcinomas and squamous-cell carcinomas of the lung, mesotheliomas of the pleura and, occasionally, mesotheliomas of the peritoneum. However, animal experiments did not confirm the findings from epidemiological

studies that tumours may also develop in the gastrointestinal tract after asbestos inhalation. Important quantitative information was provided by Davis et al. (1978, 1980), IARC Symposium (1987), Reeves et al., (1974), Wagner et al. (1974), and a recent WHO/IPCS document (IPCS, 1986). Based on this information, the following statements can be made.

- The lung cancer incidence in rats after inhalation of asbestos is approximately linearly related to the fibre concentration in air and the length of exposure.
- Mesotheliomas, however, are observed relatively frequently among rats exposed either for a short period to asbestos (after a long latency period), or to low asbestos concentrations. This suggests that a linear dose-response relationship is less likely for mesotheliomas. This has been confirmed by studies on humans occupationally exposed to asbestos, in which the incidence of mesotheliomas did appear to be linearly related to the fibre concentration, but exponentially related to the duration from first exposure (see 6.3.2.).
- Fibre length, and possibly also fibre diameter, are very important for the degree of carcinogenicity after inhalation, with longer and thinner fibres producing more tumours than shorter and thicker fibres (in similar mass and fibre concentrations). The various asbestos types, with different mineral composition, can therefore only be compared as to their carcinogenic potency after a proper description of the fibre dimensions.
- In addition to fibre dimensions and concentration, the durability of the fibres may be important. This was indicated by inhalation experiments with manmade mineral fibres, which were sometimes also able to produce small numbers of lung tumours in rats (NRC, 1984; Wagner, 1982). Chrysotile has been reported to dissolve slowly in the body whereas amphiboles remain intact. However, despite these differences in biological solubility, there are no clear indications from animal inhalation experiments that chrysotile has a lower carcinogenic potency than amphiboles (see also 6.7.).

Intratracheal studies with rats have demonstrated a strong synergistic effect of asbestos and cigarette smoke, and of asbestos and chemical carcinogens, such as polycyclic aromatic hydrocarbons, in respect of risk of lung cancer, but not of mesotheliomas (Shabad et al., 1974; NRC, 1984; IPCS, 1986).

Asbestosis is a characteristic fibrosis of the lung, which begins as an inflammation-like reaction in and around the terminal bronchioles where fibre-containing macrophages accumulate, and then gradually progresses into a diffuse focal fibrosis of the lung interstitium and the pleura. Severe asbestosis causes impaired lung function and partial or sometimes even complete obstruction of the airways (Begin et al., 1983; Glassroth et al., 1984). This fibrosis develops slowly, but is an irreversible process, often even after cessation of exposure.

Asbestosis has been reported to occur in all animal species after inhalatory exposure to asbestos (both short- and long-term) and after single or repeated intratracheal asbestos administration (Reeves et al., 1974; Wagner et al., 1973; Wehner et al., 1979; Begin et al., 1982, 1983). As with carcinogenesis, the severity of the fibrotic reaction also depends on the amount and the length of the fibres (Davis et al., 1978; Reeves et al., 1974; IPCS, 1986), but a linear dose-response relationship is less likely here. The time from onset of exposure and the duration of exposure are both important factors determining the degree of fibrosis occurring in rats (Wagner et al., 1974). Intermittent exposure for short periods of time to high asbestos concentrations produced more severe asbestosis than more continuous inhalation of the same cumulative dose (Davis et al., 1980).

Non-asbestos fibres can also produce asbestosis in rats in a dose-related manner, but the response is usually lower than with asbestos at similar mass concentrations (Lee et al., 1982; Wagner, 1982). The lowest reported concentration studied in animals (1 mg chrysotile with 99% fibres shorter than 5 μm and a concentration of 3000 fibres longer than 5 μm per litre of air) did not cause any fibrotic reaction after lifelong inhalation (Platek et al., 1985). The same mass concentration of chrysotile with a higher number of fibres longer than 5 μm (1.3×10^4 fibres per litre of air) produced mild fibrosis in hamsters after 15 months inhalation (Wehner, cited by IPCS, 1986). In the latter study, no indication was given of the fibre size distribution.

6.2.3. Intrapleural/intraperitoneal studies

Intraperitoneal and intrapleural studies with asbestos and related materials have mainly been conducted to investigate the importance of fibre size and shape in the induction of mesotheliomas. Different groups of researchers arrived at basically the same conclusions.

Mesotheliomas can be induced in rats by a variety of durable fibrous materials, including asbestos, after intrapleural or intraperitoneal administration. The probability of tumour formation seems to be a continuous function of both the length and the diameter of the fibres, and relatively independent of the type of material. Fibres with a length of 20 μm or more and a diameter of 0.1-0.25 μm probably have the highest relative carcinogenic potency, which decreases with a decreasing length and/or an increasing diameter of the fibres (see figure 5.1.). The risk of fibres with a length of < 5 μm and/or a diameter of > 2 μm, which may still have some carcinogenic potency according to this theory (Pott, 1978; Stanton et al., 1981), is believed to be zero by many investigators (Wagner et al., 1973; Wagner, 1982), and will in any case be negligible in practice. There are no indications from intrapleural and intraperitoneal studies that chrysotile and amphiboles differ in their carcinogenic potencies. However, chrysotile from which more than 80% had been removed by acid treatment (to simulate the leaching of chrysotile in the body) induced fewer tumours than did untreated chrysotile in rats following intrapleural inoculation (Monchaux et al., 1981). Modified chrysotile (treated with $POCl_3$ at high temperatures) had a lower carcinogenic potency than normal chrysotile after intraperitoneal injection (Maltoni, IARC Symposium, 1987).
As regards asbestosis, the results of intrapleural and intraperitoneal studies confirmed those of inhalation experiments; short fibres, of both asbestos and non-asbestos materials, are less fibrogenic than longer fibres of the same material (NRC, 1984; IPCS, 1986). However, the investigations into the critical fibre dimensions for fibrogenesis are not as extensive as for carcinogenesis. Some researchers suggest that asbestos-related lung cancer is always preceeded by a fibrotic condition of the lungs (Kuschner, 1982, 1986). Others believe that both processes proceed independently (WHO, Copenhagen, 1986). Despite the similarity in the fibre dimensions involved in the two processes, there is as yet no evidence from animal studies that they are directly related.

6.2.4. Reproduction/teratogenicity

Asbestos can cross the placenta of rats, as was demonstrated by intravenous injection (Cunningham and Pontefract, 1973). However, only one study investigating the possible effects of asbestos on embryonic development has been published. The average number of implants in mice receiving daily

approximately 0.4, 4 or 40 mg chrysotile per kg body weight in drinking water during pregnancy was slightly smaller in the lowest dosage group than in the other groups. This was not considered to be treatment-related. In vitro exposure of mouse blastocytes to 1, 10 or 100 μg chrysotile.ml^{-1} did not affect the development of the blastula in vitro but did produce a dose-related increase in the number of dead and resorbed foetuses after implantation (Schneider and Maurer, 1977).

6.2.5. Mutagenicity

None of the commercial asbestos varieties had mutagenic properties in bacterial systems (Chamberlain and Tarmy, 1977; Szyba and Lange, 1981). One natural asbestos type was found to be mutagenic in a reverse mutation test with Escherichia coli CSH50, but this was probably due to contamination (Cleveland, 1984).

In in vitro mammalian systems, all tested asbestos varieties were able to induce chromosomal aberrations, consisting of numerical as well as structural changes, including exchanges (Hesterberg and Barrett, 1985; Huang et al., 1978; Lavappa et al., 1975; Oshimura et al., 1984; Price-Jones et al., 1980; Sincock and Seabright, 1975; Sincock, 1977, cited by EPA, 1985; Valerio et al., 1983). These chromosomal abnormalities may be a direct result of physical interaction of asbestos fibres with chromosomes and/or structural proteins of the mitotic apparatus. The transformation of cells, which was also frequently reported after in vitro exposure to asbestos, may be directly related to this mechanism (Hesterberg and Barrett, 1985). One study reported weak mutagenic action of asbestos at the HPRT locus in CHO cells (Huang et al., 1978; Huang, 1979), but this could not be confirmed by various other authors (Newman et al., 1980, cited by EPA, 1985; Oshimura et al., 1984; Reiss et al., 1982, 1983). The reported mutagenic action was probably secondary to cytotoxic damage. Tests in which the induction of single and double strand DNA breaks in animal and human organ cultures, and the induction of repair of DNA damage (unscheduled DNA synthesis, UDS) in human fibroblasts (EPA, 1985) and rat hepatocytes (Denizeau et al., 1985) were examined, also gave negative results. However, one type of erionite (a naturally occurring fibrous material which is extremely potent in inducing mesotheliomas in rats after inhalation) did cause increased UDS in both human and murine cell lines (Poole et al., 1983).

Only two in vivo mutagenicity studies have been published, in mice and in monkeys. The results of a single oral or intraperitoneal administration of chrysotile were negative in both species (Lavappa et al., 1975). Although there is no conclusive evidence of an increased sister chromatid exchange (SCE) rate in in vitro animal systems (Livingston et al., 1985; Casey, 1983), data from studies with humans occupationally exposed to asbestos suggest a weak relationship between asbestos exposure and SCE rate, which is greatly enhanced by cigarette smoking (Rom et al., 1983a). A striking increase in mutagenicity in bacterial and in vitro mammalian systems was also observed after simultaneous treatment with asbestos and benzo(a)pyrene, but not with several other chemical mutagens or with UV radiation (Szyba and Lange, 1982; Reiss et al., 1983; DiPaolo et al., 1983; Denizeau et al., 1985; Mossman et al., 1984a).

6.2.6. in vitro toxicity

Various authors have reported that asbestos has a haemolytic effect on blood from humans and several animal species in vitro, which is an indication of interaction with cell membranes. Chrysotile is more potent than amphiboles as regards this effect. Fibre dimensions are probably not important here, since the effect is caused by surface characteristics (Beck and Tilkes, 1980; Brody et al., 1983).

The cytotoxicity of asbestos fibres to a variety of mammalian cells in culture, as measured by the inability to form colonies or by an increased membrane permeability, is related to fibre size. Longer fibres are generally more toxic than shorter fibres (Beck and Tilkes, 1980; Tilkes and Beck, 1982; Chamberlain et al., 1982). The toxicity of asbestos fibres to phagocytizing cells may be due to incomplete phagocytosis. The resulting increased permeability of the cell membrane, leading to the release of lysosomal enzymes and toxic cell metabolites such as oxygen radicals from the cells, could be responsible for some of the pathological processes occurring in vivo.

Asbestos fibres appear to reduce the phagocytizing capacity of macrophages in vitro (Doll et al., 1982a, b; Warheit et al., 1984a, b). The migration of phagocytizing cells towards asbestos fibres was also inhibited after in vitro exposure to asbestos (Yano et al., 1984; Rola-Pleszczynski et al., 1984; Myrvik et al., 1985). In this way, the normal clearance mechanism of the lungs for foreign particles may also be suppressed in vivo by exposure

to asbestos. In vitro studies suggest that asbestos may alter the cellular immune response of organisms, both by direct interaction with lymphocytes and by activation of macrophages (Donaldson et al., 1985; Barbers et al., 1982; Bozelka et al., 1983a).
Although certain effects observed in vitro may explain some of the processes in asbestos pathology, it should be stressed that these studies do not represent the situation in vivo, and are therefore no more than an indication of the mechanisms involved.

6.3. EFFECTS ON MAN

6.3.1. Ingestion

Geographical correlation studies, relating a high asbestos concentration in drinking water to the cancer incidence or mortality in a certain region, generally suffered from serious limitations, some of which were inherent to the type of study (Marsh, 1983; Erdreich, 1983). These inherent factors included non-correction for occupational exposure to asbestos (for example, Wigle et al., 1977; Toft et al., 1981), which is probable why positive associations were observed in men and hardly ever in women in these studies. In many studies the average duration of exposure to asbestos at the time of observation was shorter than the latency period for asbestos-related cancers (Marsh, 1983; Levy et al., 1976; Sigurdson et al., 1982; Sigurdson, 1983; Millette et al., 1983b; Harrington et al., 1978; Meigs, 1983; Sadler et al., 1984). In some studies the estimated exposure levels were very low (Millette et al., 1983b; Harrington et al., 1978; Meigs, 1983; Sadler et al., 1984), which means that negative results cannot be extrapolated to possibly higher exposure situations. However, since these low exposure levels are probably representative of areas with asbestos cement pipes as the only source of fibres in drinking water, the results may reflect the absence of a risk to the communities in such areas.
A series of studies potentially valid with respect to duration and intensity of exposure and size of the study population (in the San Francisco Bay Area in California by Kanarek et al., 1980; Conforti et al., 1981; Tarter, cited by Marsh, 1983; Conforti, 1983; Kanarek, 1983; Cooper, 1983) suggested a positive association between asbestos ingestion and gastrointestinal cancer, especially of the stomach and pancreas. However, these effects may have been the result of occupational exposure to

asbestos, which could not be excluded in this region. Another potentially valid series of studies, in the Puget Sound region in Washington, USA, did not show any association between asbestos in drinking water and these forms of cancer (Severson et al., cited by Marsh, 1983; Polissar et al., 1982). Only one case-control study has been reported, which did not find a relationship between asbestos exposure and cancer of the digestive tract and related organs (Polissar et al., 1983, 1984).

6.3.2. Inhalation

Carcinogenic effects

There is sufficient evidence that asbestos is carcinogenic in humans after inhalation. All five commercial asbestos varieties (chrysotile, crocidolite, amosite, anthophyllite and tremolite) have been linked to lung cancer and mesotheliomas of the pleura and peritoneum (EPA, 1985; IARC, 1982). Of 41 studies of cohorts occupationally exposed to asbestos, 30 showed an increased standardized mortality ratio (SMR) for lung cancer which was statistically significant at the level of $p = 0.05$, varying from 1.25 to 8.75. The relatively large variability may be the result of different exposure levels in the different occupational groups, of different types of fibre, and so on. Mortality from pleural mesotheliomas occurred in 30 of the 41 studies (in 23 out of the 30 studies that were positive for lung cancer). Mortality from peritoneal mesotheliomas occurred in 21 of the 41 studies (in 19 out of the 30 studies that were positive for lung cancer). However, many peritoneal mesotheliomas may have been misdiagnosed as cancer of the pancreas or other sites (Selikoff et al., 1979). See also table 6.1.

Table 6.1. Mortality from mesotheliomas in 41 cohort studies (EPA, 1985)

Fibre type to which the cohort was exposed	*Number of studies*	*Mortality*, % of total mortality (n=no. of studies with mesotheliomas >0)*	
		Pleural mesotheliomas	*Peritoneal mesotheliomas*
Chrysotile only	*9*	*0.3-1.2% (4)*	*0.2- 0.4% (2)*
Predominantly chrysotile	*6*	*0.3-3.1% (6)*	*0.5- 2.4% (4)*
Amosite	*2*	*1.2-1.3% (2)*	*0.3- 1.3% (2)*
Predominantly crocidolite	*5*	*1.4-7.8% (5)*	*0.9-11.3% (8)*
Mixed asbestos	*16*	*0.6-8.3% (12)*	*3.5- 6.9% (8)*
Anthophyllite	*1*	-	-
Talc (with tremolite)	*2*	-	*0.9% (1)*

** The mortality from mesotheliomas in the general population is very low (<0.04% of total mortality in the USA)*

The relative lung cancer risk (observed/expected) appears to be independent of age. The excess risk (observed - expected) for mesotheliomas (which can be equated to the absolute risk because the incidence of mesotheliomas in the general population is very low) is also independent of age. However, the excess risk for lung cancer shows a linear relationship with age. The relative lung cancer risk increases approximately linearly with the time from onset of exposure, with a latency period of about 10 years; the risk of mesotheliomas, however, increases exponentially with the time from initial exposure. There is a sudden decrease in both lung cancer and mesotheliomas 40 to 50 years after onset of exposure, which is only partly understood (Selikoff et al., 1979; Seidman, 1984).

The risk of both lung cancer and mesotheliomas is probably linearly related to the fibre concentration in the air. However, since in most studies the fibre concentration was not measured directly but calculated from mass measurements or total particle counts, the degree of exposure to fibres as established for these studies can only be a rough estimate. Whereas some researchers believe that the existence of a linear relationship between fibre concentration and tumour incidence is only speculative, and that a quantitative risk estimate based on such inaccurate data is not possible (IPCS, 1986; IARC Symposium, 1987), others applied linear regression models to describe the relationship between the observed mortality from lung cancer in the various cohorts and the estimated cumulative exposure (Liddell and Hanley, 1985; EPA, 1985). At a recent IARC symposium it was confirmed that, despite all objections, a linear non-threshold extrapolation model seems, at the moment, the most appropriate model for a quantitative risk assessment of low exposure levels (Doll, IARC Symposium, 1987). The effects of asbestos exposure and smoking appear to be approximately multiplicative. The death rate from lung cancer in a large cohort of asbestos workers, for example, was about five times higher than expected for both smokers and non-smokers. Since smoking by itself caused a 10-fold increase in lung cancer mortality, the mortatility from lung cancer among asbestos-exposed smokers was 50 times higher than among non-asbestos-exposed non-smokers (Hammond et al, 1979). No multiplicative effect of smoking was observed for mesotheliomas. There is no evidence for differences in response between the different asbestos types with respect to lung cancer (EOA, 1985). However, the data from cohort studies suggest that as regards the development of mesotheliomas the amphiboles, especially crocidolite, are more potent than chrysotile (see table 6.1.). This appears

to be confirmed by recent autopsy studies of lung material from mesothelioma patients. For example, the number of fibres in the lungs of mesothelioma patients who had been working in the chrysotile industry was up to 400 times higher than the number of (amphibole) fibres in the lungs of patients previously employed in the amphibole-processing industry (Churg and Wright, IARC Symposium, 1987).

In 10 out of the 23 occupationally asbestos-exposed cohort studies statistically powerful enough to detect an increased risk of gastrointestinal cancer mortality, the observed excess of deaths was significant at the level of $p = 0.05$. There appears to be a constant relationship between increased mortality from gastrointestinal cancer and from lung cancer (EPA, 1985). Because of the lack of confirmatory data from animal experiments and the absence of a dose-response relationship, some authors ascribe the observed rise in the incidence of gastrointestinal cancer entirely to misdiagnoses (gastrointestinal cancer instead of lung cancer or mesotheliomas; EPA, 1985; IPCS, 1986). The EPA Cancer Assessment Group concludes that the evidence of a causal relationship between asbestos inhalation and gastrointestinal cancer is strong, but the WHO considers this evidence to be weak, and concludes that "the risk to the general population is very small, if any" (WHO Air Quality Guidelines, 1987). Although a causal relationship between asbestos inhalation and gastrointestinal cancer cannot therefore be excluded, the risk of gastrointestinal cancer will in any case always be lower than that of lung cancer, so that it will have no effect on the final risk estimate for the purpose of setting an asbestos standard for the general population. It must be stressed that the possible carcinogenic activity of asbestos in the gastrointestinal tract after inhalation does not imply that asbestos may also be carcinogenic after ingestion.

Other tumours were sometimes also slightly increased in occupationally exposed cohorts, but there is no evidence of a causal relationship with asbestos (EPA, 1985; IPCS, 1986).

There are strong indications that household contacts of asbestos workers have an increased risk of lung cancer and mesotheliomas (Anderson et al., 1976; Glickman et al., 1983). These data appear to be substantiated by the measurements of several times higher fibre concentrations in the homes of chrysotile miners compared with non-miners (Nicholson et al., 1980; IPCS, 1986). The risk of mesotheliomas was also found to be increased for individuals who live in the neighbourhood of asbestos mines or factories

(IPCS, 1986). The above cases are sometimes mentioned as examples of effects occurring at low exposure levels. However, the concentrations in the homes of asbestos workers and near asbestos mines and factories were in the past many times higher than the concentrations currently permitted in occupational situations, so that they can hardly be regarded as low exposure levels.

Direct dose-response data concerning very low-level exposures are not available. Data on the mortality from mesotheliomas (regarded as a fairly good indicator of exposure to asbestos because it has no other known causes) in Canada, the USA, Norway, Finland and the UK suggest, however, that exposure to "background" levels of asbestos does not contribute appreciably to the risk of mesotheliomas and lung cancer. Since the start of the industrial application of asbestos in the fifties, when the mesothelioma incidence was very low and identical for men and women, the mesothelioma incidence among men (including a high proportion of occupationally exposed) has risen sharply, whereas that among women ("background" level exposure) hardly changed during the last 10 to 20 years (McDonalds, IARC Symposium, 1987).

Asbestosis

Analysis of clinical and X-ray symptoms and signs of asbestosis in workers of an asbestos textile factory suggested that the risk of developing asbestosis is less than 1% from a cumulative exposure of 0.7 fibres per ml of air for 40 years (=28 f-y/ml; Berry et al., 1979). Other analyses among the workers of asbestos factories indicated a risk of radiographic abnormalities of < 2% at a cumulative exposure of 25 f-y/ml (EOA, 1985).

The significance of minor X-ray changes is not clear. They may or may not be associated with reduced lung function. The significance of these abnormalities in relation to lung cancer is likewise obscure. Asbestosis as the cause of death has frequently been reported among occupationally exposed cohorts, but never in groups exposed to lower concentrations (EPA, 1985). Asbestosis mortality in heavily exposed workers appears to be related to the estimated duration and intensity of exposure and the time since first exposure (IPCS, 1986). However, it is not known whether the generalized progressive fibrosis exhibits the same linear relationship. Therefore, extrapolation from occupational situations to low exposure situations is not possible.

The above observations indicate that asbestosis at low levels of exposure does not appear to be an important problem, but that the primary risk consideration at those concentrations should be the carcinogenic effects (EPA, 1985; IPCS, 1986).

6.4. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

Toxicity to aquatic organisms

Little attention has been paid to the effects of asbestos on aquatic systems. The few studies that are available - mainly laboratory studies - indicate that asbestos fibres are taken up by algae, molluscs and fish, and are able to cause morphological changes in those organs of fish that are involved in the uptake and concentration of fibres from water (gills, kidneys) at relatively high concentrations (10^8 fibres.l^{-1}; Laut and Schurr, 1984; Woodhead et al., 1983; EPA, 1980). In one study, asbestos inhibited the growth and reproduction of Asiatic clams at concentrations of 10^2-10^4 fibres.l^{-1} and higher (Belanger et al., 1986). The limited amount of data does not permit any conclusions about the effects of asbestos on ecosystems.

6.5. EFFECTS ON MATERIALS

The principal effect of the deposition of particulate air pollutants onto material surfaces is that these become dirty. In addition, deposited particles can cause direct (e.g. through action of the water-soluble fraction) and indirect (e.g. through absorption of moisture and reactive gases, and catalytic activity) chemical degradation.

The last-mentioned effects depend heavily on the physical and chemical properties of the deposited particles. Since asbestos fibres are relatively inert in physico-chemical terms, direct and indirect chemical effects are considered to be of minor importance. The only remaining, but not very asbestos-specific, effect is that of fouling.

Since the mass concentration and deposition of asbestos, even in the immediate vicinity of sources, are small compared with the total particulate load (1% or less), fouling by particles other than asbestos will dominate.

6.6. EFFECTS ON A GLOBAL SCALE

In view of the expected low atmospheric asbestos concentrations in areas far removed from sources, the contribution of asbestos to the known effects of air pollution on a global scale (such as cooling of the atmosphere by reflection of radiation back into space) will be of minor importance.

6.7. SUMMARY AND EVALUATION

Only a very small proportion of ingested asbestos fibres will cross the gastrointestinal wall and be excreted into the urine; only few fibres will penetrate into the tissues and be retained there. The major part of ingested asbestos will be excreted into the faeces. With respect to the inhalatory route, it can be concluded that respirable asbestos particles with a Dae of 0.1 to 0.2 μm, and independent of fibre length, have a high possibility of reaching the alveolar regions of the lungs, from which they are only very slowly cleared. Many uncleared particles will migrate towards the periphery of the lung and to the pleura. Chrysotile fibres are probably partly dissolved during their residence in lung tissue, whereas amphibole remain there largely intact.

The available animal studies with asbestos do not demonstrate an increased risk of gastrointestinal tumours in rats and hamsters after lifetime ingestion. Other tumours that were sometimes slightly increased were often also found in untreated animals and/or were not increased in other comparable studies; they are therefore not considered to be treatment-related.

The critical effect of asbestos to the general population is cancer. The results of animal experiments with oral exposure to high asbestos fibre concentrations are essentially negative. The results of epidemiological studies relating asbestos exposure via drinking water to health effects are in some cases negative. In other cases there is a suggestion of a possible relationship with an increased incidence of gastrointestinal tumours. However, there is a strong possibility of occupational and/or environmental exposure in these studies, which may explain the positive correlations found.

Studies of occupationally exposed cohorts, in which exposure to asbestos has mainly been inhalatory, sometimes also suggest an increased risk of

gastrointestinal cancer. Although the evidence must be regarded as weak (animal experiments did not confirm this risk, and some researchers attribute it to misdiagnoses of what were in fact peritoneal cancers), a causal relationship between asbestos inhalation and gastrointestinal cancer cannot be excluded. However, this possibility does not necessarily imply that asbestos may also be carcinogenic after ingestion, because of the differences in fibre dimensions and concentrations, and thereby in biokinetics and biological activity of the different fibres involved.

Since the evidence that asbestos may be carcinogenic after ingestion is very weak, the risk of cancer from ingested asbestos is considered negligible at the current exposure levels. Therefore, a health-based limit value for asbestos in food and drinking water is not proposed.

Inhalatory exposure to asbestos is associated with cancer. Both animal experiments and epidemiological studies have provided sufficient evidence that inhalation of asbestos results in lung cancer and mesotheliomas. A number of studies of occupationally exposed groups indicated an increased incidence of gastrointestinal cancer, but this was always much smaller than the increase in lung cancer incidence. For a risk estimate, lung cancer and mesotheliomas can therefore be regarded as the critical effects of asbestos inhalation.

The risks of lung cancer and mesotheliomas have to be assessed separately because of the different dose-response relationships. Lung cancer is linearly related to the cumulative exposure, whereas mesotheliomas appear to be linearly related to fibre concentration but exponentially related to the time since first exposure.

The carcinogenic potency of asbestos appears to be a function of the fibre dimensions which can vary for the different types and brands of asbestos, depending on origin, type of processing, application, etc. Inhalation and intrapleural/intraperitoneal anumal studies show that chrysotile and the various amphiboles do not differ in carcinogenic potency as long as the fibre dimensions and concentrations are similar. On the other hand, mesotheliomas are less frequently observed in epidemiological studies with exposure to chrysotile only, than in studies in which exposure was to predominantly amphiboles or to both amphiboles and chrysotile. The difference between animal and epidemiological studies may partly be explained by the fact that chrysotile slowly dissolves during its residence in the tissues whereas amphibole fibres remain intact and accumulate in the periphery of the lungs and in the pleura. This would account for a lower expression of the carcinogenicity of chrysotile in humans compared with

much shorter-living laboratory animals. However, it is not possible to compare epidemiological data obtained from different types of industry involving fibres of widely different dimensions. The fibre dimensions were not given in any of these studies. The results of recent autopsy studies are therefore relevant. These studies, with lung material from mesothelioma patients who had been employed in different asbestos-processing industries, confirmed that chrysotile can induce mesotheliomas in humans, but probably in much higher fibre concentrations than the amphiboles. Doll and Peto (1985; IARC Symposium, 1987) proposed as a working hypothesis a 20x lower potency of chrysotile than for the amphiboles. With respect to the induction of lung cancer, chrysotile and the amphiboles do not appear to differ substantially.

The upper limits of the respirability of fibres are a fibre diameter of about 3 μm and a fibre length of about 200 μm. Strictly speaking, "safe" fibre dimensions within these limits of respirability cannot be given because carcinogenicity is considered to be a continuous function of fibre length and diameter. In practice, however, the risk from fibres shorter than 5 μm will be negligible, and these will therefore not be considered in the risk evaluation.

Since no dose-response data are available for very low asbestos exposure levels, the quantitative risk evaluation will be based on epidemiology from occupationally exposed humans. Fibre concentrations in work situations were usually not directly measured, but estimated from mass measurements and total particle counts. These estimates were based on optically visible fibres. An optical microscope (OM), with a detection limit of about 5 μm fibre length and 0.3 μm fibre diameter, was also used whenever direct fibre measurements were made. The much lower fibre concentrations in the environment are, however, determined by electron microscopy (EM). To compare OM and EM concentrations of fibres longer than 5 μm, a conversion factor must be used. A factor of 2 seems realistic for conversion of occupational levels to ambient air asbestos levels (WHO Air Quality Guidelines, 1987; Cherrie, IARC Symposium, 1987).

The risk of lung cancer is about ten times higher for smokers than for non-smokers, and is multiplicative to the risk from asbestos exposure. The risk of mesotheliomas is not influenced by smoking. Since so many uncertainties are involved in a quantitative risk evaluation for environmental asbestos levels, resulting in a wide range of possible risks, it is not considered scientifically appropriate to calculate a separate risk figure for non-smokers in the general population. The risk assessment by the WHO working

group for Air Quality Guidelines (1987), which - with modifications - has also been adopted in this Integrated Criteria Document, applies to the general population with approximately 30% smokers.
A description of this risk assessment can be found in the WHO working document of the WHO Air Quality Guidelines (1987), and is also given in Appendix I to this chapter. In the WHO Air Quality Guidelines, an excess lung cancer risk was given in the range of 10^{-6} to 10^{-5} for a population with about 30% smokers, and a mesotheliomas risk was given in the range of 10^{-5} to 10^{-6} for smokers and non-smokers, for lifelong exposure to 500 opticaly measured fibres per m^3, for all asbestos types. In this Integrated Criteria Document, an order of magnitude of 10-100 will be applied for the difference between amphiboles and chrysotile with respect to mesotheliomas (in accordance with the previously mentioned factor of 20). The ranges of risk for lung cancer and mesotheliomas given by the WHO Guidelines will be translated into ranges of exposure levels that can be associated with lifetime risks of 10^{-6} and 10^{-4}, respectively.

Table 6.2. Risk estimate for the general population

Effect	*Lifetime risk*	*Lifetime exposure to*	
		Fibres/m3 measured by OM	*Fibres/m3 longer than 5 µm measured by EM**
Mesotheliomas (for smokers and non-smokers-	*1/10⁶*	*5- 50 (amphiboles)*	*10- 100*
		50- 5,000 (chrysotile)	*100- 10,000*
	1/10⁴	*500- 5,000 (amphiboles)*	*1,000- 10,000*
		5,000-500,000 (chrysotile)	*10,000-1000,000*
Lung cancer (for a population with 30% smokers)	*1/10⁶*	*50- 500*	*100- 1,000*
	1/10⁴	*5,000- 50,000*	*10,000- 100,000*

** Calculated with a conversion factor of 2*

It must be stressed again that the figures in this table only give an indication of the possible risks, but because of the conservative assumptions made, they will provide adequate protection of public health.
With respect to ecosystems, the data available are insufficient to make recommendations possible. The negative effects of asbestos on materials are limited; the contribution is negligible compared to other components with similar polluting effects. Effects on a global scale are neglectible.

7. EMISSION REDUCTION AND COSTS

7.1. PRESENT SITUATION

Since the seventies there has been a continuous trend towards limiting the application of asbestos and the emissions arising from its use. Statutory measures in the Netherlands as well as abroad prohibit various applications of asbestos (Asbestos Decree, 1977, 1983). As a result, there has been a sharp fall in the production and use of asbestos and asbestos-containing products (subsection 2.1.2.). Asbestos-free corrugated sheets of adequate quality are available but are not yet extensively used. A number of car manufacturers have fitted their new models with asbestos-free brake linings and clutch facings. The proportion of asbestos-free brake linings, etc., used in the replacement of brake parts is still small. Asbestos-free material is used to a limited extent in brakes of buses, trucks and trailers. The car industry in particular is still hesitant because of doubts about the required high quality (VROM, 1985). Application of alternatives to asbestos in industrial friction materials is technically not yet feasible. Asbestos-free packing and gaskets, having the same resistance as asbestos-based ones, are available for a number of applications, but are expensive.

As a result of the decrease in production and use as well as the extensive control measures taken in the remaining processing of asbestos and asbestos-containing products, the emissions have also fallen sharply.

The volume of asbestos-containing waste products has also declined, and increasing attention is being paid to the re-emission problem caused by their dumping.

7.2. AUTONOMOUS DEVELOPMENTS

The estimates given in chapter 2 show that the largest emissions arise from sources which are very diffuse and difficult to control, which hampers emission reduction. Major sources are the result of asbestos application in durable materials, especially in the construction industry. Even if application of these materials were to cease tomorrow, the materials already in place continue to be a long-lasting source of asbestos emissions.

In the next few decades, asbestos dumping will increase owing to the presence of more asbestos in buildings that are due for renovation or demolition (SVA, 1978; table 2.6.). The extent and rate of replacement of asbestos-containing materials by asbestos-free alternatives largely determine the development of the future asbestos emissions. Substitution influences the magnitude of the emissions in two ways:

- because of the accelerated pace of removal of asbestos-containing materials (for example, sprayed asbestos insulations), there will be a large increase in the emission for the duration of such a programme;
- the emission of asbestos fibres from the large diffuse sources will fall sooner.

Table 7.1. lists the anticipated emissions in the coming decades. It has been assumed here that, first, the production of asbestos-containing bitumen and coatings will cease in addition to that of asbestos-containing flooring, insulation, packing and gaskets. Secondly, the number of cars increases by 150,000 annually while the contribution of asbestos-free brake linings will remain small for the present. The other consumption and production figures are supposed to be constant.

Table 7.1. Autonomous development of asbestos waste streams and emissions into water and air

	1982	*1985*	*1990*	*2000*
Amount of asbestos in waste (tonnes per year)				
- practically unbound asbestos	*580*	*530*	*530*	*30*
- bound asbestos	*2230*	*1335*	*1420*	*1580*
- asbestos in large waste streams (incl. building and demolition waste)	*1580*	*1720*	*2020*	*5120*
Emission into water, total (kg per year)	*2710*	*2160*	*2160*	*2160*
Emission into air (kg per year)				
*- brake dust on roads**	*600*	*660*	*750*	*950*
- building demolition/rubble breaking	*280*	*305*	*350*	*900*
*- brake dust in garages**	*365*	*390*	*340*	*420*
- other sources	*1030*	*1030*	*1030*	*1030*
Total	*2275*	*2385*	*2470*	*3300*

** assuming that penetration of asbestos-free brake linings is very gradual*

7.3. SUBSTITUTION OF ASBESTOS

Possibilities and costs

The most effective way to limit the emissions is the replacement of asbestos by alternative reinforcing fibres. Several studies have shown that substitute materials can be used in many instances (EPA, 1980; Green and Pye; VDI, 1982; VROM, 1986).

According to Köhling et al. (1986), a substitute is technically possible in principle for nearly all applications of asbestos except for a few very specific uses, such as:

- electrical insulation for mechanically heavily loaded cables
- asbestos cement lining in very large arc chambers
- electrical collectors
- surface coating in very acid or high temperature environments
- gaskets in very hot gas environments
- diaphragm electrolysis process (entirely different processes for electrolysis do exist in which asbestos is not required)
- pressure pipes for drinking and waste water

Direct substitution is not always possible in parts such as brake linings and the like, or in parts which are produced according to technical specifications laid down for a long time (e.g. in the aviation industry). Substitution will often require far-reaching intervention in the technical design and construction of appliance parts. A less drastic measure aims at less tightly bound asbestos in products and lower asbestos contents in products in which asbestos cannot yet be dispensed with entirely. The introduction of asbestos-free products is hampered by the often higher price of substitute materials, the necessary technical modification of entire systems, and doubts about the durability of the substitute materials. As a result, long introduction and transition periods are needed when asbestos-free alternatives have in principle been chosen. Information about the non-recurring costs of substitution is not available and has therefore not been included in the calculation.

Alternatives for asbestos cement

The cost price of cement sheet with different fibre reinforcement is about 15% higher owing to the more expensive reinforcing material (aramide, cellulose, etc., 30% higher compared with asbestos) and modifications to the production processes (about 10% higher compared with the current production method). It is not yet known how durable this material is; any extra costs arising from a possibly shorter life have therefore not been included in the calculation. Modifications of treatment and processing methods may involve some initial expenditure, but has no cost-raising effect in the long run. On the basis of this information, it can be calculated that the extra costs incurred per year will be f 28.5 million, assuming:

- complete substitution of asbestos cement sheet, corrugated sheet, etc. (but excluding pipes)
- an average price of these products of about f 1.- per kg product
- an annual consumption of 95 ktonnes (table 2.3.), and
- an average cost price rise of 15%

This cuts the emissions by about 650 kg per year after a period of a few decades.

Alternatives for asbestos in braking and friction materials

Because of the broad range of applications and technical possibilities of substitution, a distinction has to be made between application in brake pads and brake linings for passenger cars, brake shoes for lorries, buses and trailers, clutch facings, and industrial friction materials (in elevators, cranes, etc.). Brake pads, brake shoes and brake linings are by far the largest sources of asbestos emissions, so only their substitution will be explained in more detail.

The price of asbestos-free braking materials for passenger cars is about 50% higher, and that for lorries, buses, trailers, etc. about 80%. Based on an annual consumption of 1.6 million sets of braking pads and 0.55 million sets of brake linings for passenger cars, and 0.22 million sets of brake shoes for heavy transport, the additional annual costs incurred by the use of asbestos-free braking materials would be some f 80 million. These braking materials have been reported to last 1.5 to 2 times as long as the traditional materials. Although the cost price per unit will thus be higher, the annual costs are much lower, while savings are also made on maintenance and repair. The additional costs for asbestos substitution in these applications would then be small or even zero.

As far as is known, braking materials without asbestos are currently being replaced much more rapidly than was anticipated for a variety of reasons, such as "shrieking" of the brakes, unfamiliarity, etc. Therefore, it is not yet possible to estimate what the actual cost will be either now or in the future when more experience has been gained with these materials. In practice, technically usable asbestos-free braking materials are available for part of the fleet of (passenger) vehicles. They are incorporated as a standard component in a number of new models. The percentage of the asbestos-free products in the replacement of brake parts is small, which can be partly attributed to their higher cost and the little experience with them to date (VROM, 1986).

For industrial friction materials, substitution by asbestos-free alternatives is technically still unforeseeable.

Alternatives for asbestos in packing material

Asbestos-free packing materials are available for most applications. Several substitute materials must be chosen for each application, but they cost approximately 3 to 4 times as much and are not as durable as the traditional products. The additional costs for substitution amount to f 6.5 million per year, assuming that:

- consumption of packing material in the Netherlands is 225 tonnes per year (in 1982)
- the cost price of asbestos-containing sheet is f 5.- to f 10.- per kg
- the cost price rises by a factor of 3 to 4, and
- the useful life is shortened by 20-50%

Any expenditure for modifications to the installations in which these packings are used and any costs for increased maintenance have not been included.

Alternatives for asbestos in other products

Very little or no asbestos is now used in the other products for insulation, fire protection, heat resistance, floor covering, etc. Asbestos has been replaced by a whole range of entirely different products, or comparable products with another fibre type, so a cost comparison is not very useful.

7.4. EMISSION REDUCTION INTO THE SOIL

7.4.1. Measures

The emissions into the soil arise mainly from the dumping of solid waste (table 2.12.). Within the three types of asbestos-containing waste streams described, a further distinction can be made into production waste, sludge from sedimentation basins, dust from cloth filters, etc., with each case requiring a different approach.

Measures designed to cut the volumes of waste per process or source through recycling, fewer rejects, etc. have only a small impact on the amount of asbestos used. Whatever its application, asbestos will eventually end up in

a waste stream. There is in fact only one measure by which the asbestos-containing waste stream can be effectively reduced, and that is substitution by alternative materials.
Reduction of the emissions into the soil from deposition and infiltration is only possible by limiting the emissions into air and water. Because of the vastly increased number of uses of asbestos-containing materials with a long life in the fifties and sixties (especially in the construction industry), the volume of asbestos-containing waste streams will increase substantially. Measures which can be taken to prevent re-emission of asbestos fibres are:
- concentration of asbestos waste streams
- "detoxification" of asbestos
- controlled transport and dumping

Concentration

Concentration of asbestos waste streams can be restricted to the prevention of asbestos-containing and non-asbestos-containing waste streams from becoming mixed, and the separate transport of asbestos waste streams to a limited number of processing and/or dumping sites. Concentration is relatively simple in production plants and in the processing industry (for example, dust from the special exhaust systems for asbestos emission control, production waste, sludge). For proper management of these waste streams, collection in separate and labelled containers is desirable. This is certainly necessary for material from which asbestos fibres are readily released (free-form asbestos, poorly locked-in asbestos and dust from cloth filters).
With diffuse sources of asbestos-containing material, concentration will involve its selective removal prior to complete demolition of a building or installation. Concentration is not possible when the asbestos is present from the outset in a diffuse and diluted form in a larger waste stream. Measures must then be taken to prevent further dissemination, such as making possible separate collection of asbestos-containing material from household and industrial waste by a warning label on materials and appliances, etc., as stipulated in the Asbestos Decree.

Detoxification

Asbestos does not disappear definitively from the environment under normal conditions. There are three methods for rendering asbestos completely

harmless, namely, immobilization, thermal decomposition, and chemical degradation. Practical application of these methods is neither desirable nor feasible for various reasons, not least because these techniques cannot effectively process materials which are not 100% asbestos.

Controlled transport and dumping

At present, there are six disposal sites in the Netherlands licenced to receive asbestos-containing waste (more than 0.5% asbestos) under the Chemical Waste Act. Licences for the dumping of construction and demolition waste as well as household and industrial waste which also contain asbestos are granted under the Waste Materials Act. The measures are aimed specifically at the first category of waste materials, and include:

- transport in closed bags, if required, in a wet state or after mixing with asbestos-containing sludge types
- containers suitable for coarse material with tightly bound asbestos
- dumping of the bags, unopened
- controlled emptying of containers
- immediate covering of the dumped material
- non-compacting of the asbestos-containing waste

Emissions into the air and the water (when a covering layer is applied immediately) do not occur then, thus preventing asbestos fibre deposition onto and infiltration into the soil.

7.4.2. Costs

The dumping of waste with tightly bound asbestos requires only a limited number of control measures, and will cost between f 40.- and f 60.- per tonne. The dumping of waste needing special attention for a variety of reasons, for example, because of poorly locked-in fibres and/or high asbestos contents, will cost approximately f 70.- to f 120.- per tonne. It is assumed in both cases that dumping on a site which complies with the guidelines for controlled disposal is possible. The cost of immobilization, when this is required because of a high concentration of free fibres, may amount to f 150.- to f 200.- per tonne. The dumping of this material will cost f 120.- to f 150.- per tonne.

7.5. EMISSION REDUCTION INTO WATER

7.5.1. Measures

The emissions into water comprise very diffuse emissions and point sources in specific production processes (table 2.13.) Emission reduction can be achieved by:

- substitution of asbestos (section 7.3.)
- collection and purification of contaminated waste water streams
- containment of asbestos
- modified work practices and processing techniques

Installation of electrolysis diaphragms and production of asbestos cement

Collection and purification is applicable to contaminated water streams occurring as point sources, which arise in the manufacture of asbestos-containing products. Free asbestos fibres can be removed from the contaminated stream by filtration and/or the addition of coagulants and flocculants in a sedimentation basin. According to the literature, waste water streams heavily contaminated with asbestos can be cleaned with a combined technique to a residual concentration of 10^5 fibres per litre (Lawrence et al., 1975). The remaining sludge must be disposed of. Further emission reduction can be accomplished by reusing the waste water as process water after treatment. Filtration is a possibility for very small waste water streams. No data exist on the residual concentrations obtained with this measure.

Weathering of floor covering and asbestos cement (outdoors)

It is conceivable to cut the emissions caused by the weathering of asbestos-containing materials by coating the surfaces with, for example, paint or wear-resistant layers. However, very large surfaces are involved on many different sites, and implementation of such measures will not be possible for both cost-technical and practical considerations.

The cost of applying paint and wear-resistant layers is expected to be of the order of f 50.- per m^2, which means an investment of nearly 15,000 million guilders for the existing asbestos cement (corrugated) sheets alone.

Modified work practices and processing techniques

It is obvious that emissions into water will no longer occur when switching from wet to dry techniques in processes, and this is also true for the cleaning of asbestos-containing flooring. However, this will probably lead to increased emission into the air. Application of closed process-water cycles limits the emission to the inevitable, but small, discharge.

The emissions from waste dumps into ground and surface waters can be substantially cut back by dumping asbestos-containing materials in packaged form and/or by the provision of a cover impermeable to water.

7.5.2. Costs

Cost of collection and purification

The cost of waste water purification by means of flocculation/coagulation and sedimentation comprises the following items of expense: sand filter beds, sedimentation tanks and dosing equipment, coagulants and flocculants (ferric chloride, polymers, bentonite) (Lawrence et al., 1975), and sludge processing.

The annual operating costs of a sand filter installation are strongly determined by the frequency of backwashing (for purification), which depends on the total content of particulates, as well as asbestos. The cost is f 0.10 - f 0.20 per m^3 of waste water for capacities ranging from 1000 to 5000 m^3 per kg. Flocculation and coagulation cost approximately f 0.25 - f 0.35 per m^3 of waste water for the same capacities.

The cost of sludge processing, thickening, dewatering, etc. is estimated to be f 25.- to f 50.- per tonne of sludge, depending on the composition of the sludge formed. The volume of sludge produced in a particular purification is entirely dependent on the total content of particulates in the waste water to be treated. It will be small when this is almost entirely asbestos.

The efficiency of purification of the waste water released when electrolysis diaphragms are installed is estimated at > 99.9%, the resulting residual emission being < 0.1 kg per year. The annual costs are 6 million guilders, i.e., f 4,500.- per kg of asbestos removed.

According to information provided by the asbestos-cement manufacturer, measures have already been taken to reduce the water emission. The resulting residual emission is reportedly now < 0.01 kg per year. The production of packing and gaskets, insulation, etc. has meanwhile ceased in the Netherlands.

7.6. EMISSION REDUCTION INTO AIR

7.6.1. Measures

The following measures will reduce the emissions into air most efficiently:
- substitution of asbestos (section 7.3.)
- collection and purification of contaminated gas streams
- concentration of activities
- containment of asbestos
- modified work practices and processing techniques

For a few sources, specific measures have a direct effect, while for other sources they are only effective in the very long term. For example, the use of filters in the processing of asbestos will have an immediate effect, whereas the replacement of asbestos in corrugated sheets by other materials will not have an effect on the emission until much later (as a result of demolition).

Collection and purification of contaminated gas streams

Collection and purification of contaminated gas streams is applicable to concentrated point sources or areas where the emissions can be concentrated into point sources. Examples are:
- space exhaust or mobile point exhaust during brake maintenance and repair in (larger) garages
- the pre-cutting to size of asbestos cement in the distribution trade
- the production of asbestos-based materials; systems which are as closed as possible are generally employed, for example, in the mixing of asbestos with other components
- the processing, trimming and after-treatment of asbestos-containing products (brake linings, gaskets)

All these measures are already being implemented, partly in response to the requirements set by the labour inspectorate. An exception is the garage sector, where only a limited number of large garages have installed a dust exhaust. The thousands of small businesses usually do not take such measures.

Point exhaust is applied when the emissions are localized inside the plant (production line, saw line, near specific equipment); space exhaust will be employed in a large room where many separate products are handled or where the activities are carried out in many areas.

Lightly loaded cloth filters are used for emission control, with removal efficiencies of > 99.9% having been reported. The load on the filter is usually less than 60 $m^3.m^{-2}.h^{-1}$. The separating action is enhanced by leaving a layer of dust on the cloth, making residual emissions of < 0.1 $mg.m^{-3}$ feasible (Guthner, 1983).
Emission values of 0.0001 kg per tonne are obtained during working with asbestos and material containing much asbestos (Lanting and Den Boeft, 1979). The residual emission values are lower, and often much lower, than the current MAC values (subsection 1.2.3.).
Domestic waste incineration may also be regarded as a point source. The flue gases contain fly ash possibly contaminated with asbestos. These flue gases are cleaned with emission-control techniques, usually electrostatic precipitators, with efficiencies of 92-99%. With more elaborate electrostatic precipitators, 99.5% separation can be achieved.

Concentration of activities

Emissions which are localized but comprise many small emissions can be controlled more effectively when they are concentrated in a limited number of areas. Examples are the processing of asbestos cement on the building site, and maintenance work on brakes in garages and workshops. Thousands of locations are concerned. In large garages, it is possible to install an exhaust unit with movable exhaust hoods, or reserve a fixed area for maintenance work on brakes. This is more difficult to realize in most small workshops. Concentration can be accomplished by equipping a number of central workshops for maintenance work on brakes.
Concentration of activities can cut the emission to 1% of the present amount when exhaust systems and effective cloth filters are installed in the central workshops.

Containment of asbestos

The reader is referred to paragraph 7.5.1. for the measures which can be taken to reduce the emission of asbestos caused by weathering of asbestos-cement wall panels, corrugated roofs and floor covering.
Sprayed insulation can be enclosed, and this will often already be the case in practice. Encasement, double ceilings and wall covering are among the possibilities. This prevents air movement and mechanical contact during use of the rooms on the one hand, and arrests a proportion of the fibres which are nevertheless released on the other. Another or additional possibility involves the application of a binder (e.g. resins) to the sprayed layer.

This method has a number of disadvantages and can temporarily increase fibre emission because of the disturbances it creates. Furthermore, the sprayed layers will eventually have to be removed, with concomitant emissions (Tempelman et al., 1985).
At present, specific asbestos waste on dumping sites is covered, to prevent emission into the air. It is essential that this is done immediately after dumping, and that the dumped waste is not further pulverized or disseminated. The wetting of material during demolition and rubble breaking, during work on brakes of motor vehicles as well as during production, can also be regarded as a form of containment.

Modified work practices and processing techniques

By adhering to a specific approach in working with asbestos-containing materials, such as using special equipment or taking appropriate measures, emissions can be considerably reduced. This approach is of particular importance for emission sources which cannot be combatted by emission-control techniques or containment (Timmermans, 1984), for example, demolition. The procedure involves:

- prior removal of all asbestos-containing materials
- dampening of any sites where asbestos is or has been present
- with high concentrations of free asbestos (sprayed insulation), closure of the area and a temporary exhaust with emission-control techniques
- transport of the material in closed bags or containers
- vacuum-cleaning of all surfaces where asbestos dust may have accumulated.

The method used for removal depends on the material. Sprayed asbestos or insulation with asbestos flock can best be sucked away; asbestos sheets should be detached and transported whole.
Special equipment exists for working with asbestos-containing materials, which causes much less dust (Teichert, 1983; Kuhner and Heimann, 1983). In addition, "wetting" is sometimes also employed to suppress dust generation. Released fibres are removed with the water.
Another important measure is the regular dedusting of floors, workclothes, equipment, roads, etc. (good housekeeping), which suppresses accumulation and re-emission of fibres.
It is estimated that emissions can be cut by a factor of 10 with modified operating practices and processing techniques.

7.6.2. Costs

The estimates are very approximate because, particularly with diffuse emissions and for activities taking place in a large number of locations, it is not possible to assess the emission conditions and how much emission reduction is required.

Collection and purification

The cost of gas purification is determined by the outlay for:

- the exhaust system with ventilator, ducts and flue
- the emission-control technique
- the modifications to the existing buildings, installations, etc.

Only lightly loaded cloth filters are recommended as an emission-control technique, with a load of less than 60 $m^3.m^{-2}.h^{-1}$. The capital outlay is relatively high because of the large cloth surface needed. The cost estimation is based on:

- capital outlay
  - . incl. cloth material, ventilator, purification system, dust collector
  - . cloth, f 160.- per m^2
  - . the installations of 300 $m^3.h^{-1}$ are easy to set up; the cost of assembling the larger installations is estimated to be 50% of that of the units
  - . for installations of 5000 $m^3.h^{-1}$, a separate flue will usually be constructed, whereby the filter is mounted on the outside, and insulation is desirable
  - . the costs, however, are exclusive of modifications to buildings and existing installations
- annual operating costs
  - . depreciation: 13% (10 years; 5% interest rate)
  - . maintenance: 2%
  - . insurance and the like: 1.5%
  - . energy consumption: 0.51 kWh per 1000 $m^3.h^{-1}$ at a pressure drop of 1.2 kPa
  - . electricity price: f 0.20 per kWh
  - . operating time: 5700 h
  - . filter life: 2 years

The outlay for point exhaust, exhaust hoods, exhaust walls and enclosed working areas with exhaust are not included, and could increase the above-mentioned costs by 10% to 100%. A figure of 30% has been assumed here.
Table 7.2. gives the capital outlay and operating expenses based on the above data for a few capacities.

Table 7.2. Costs for application of cloth filters to reduce asbestos fibre emission

Capacity (m3/h)	*Capital outlay (guilders)*	*Operating costs (guilders per year)*
300	*8*	*4*
1,000	*22*	*13*
5,000	*120*	*65*
10,000	*200*	*100*
25,000	*400*	*150*
50,000	*800*	*280*

Exhaust and gas purification systems will have to be employed in several thousand locations (in about 9000 garages, about 100 asbestos-cement processing facilities and about 60 rubble breakers). Such systems have already been installed in the still existing production plants.
On the basis of information provided by BOVAG, it is estimated that, for the cleaning of brakes, a point exhaust with a capacity of 300 $m^3.h^{-1}$ will suffice in about three-quarters of the garages. The rest will need a central unit with a capacity of 1000 $m^3.h^{-1}$ and in only a few cases of 5000 $m^3.h^{-1}$. It is thus assumed here that all garages should in principle be able to carry out work on (asbestos-containing) brakes.
An exhaust capacity of 300 to 1000 $m^3.h^{-1}$ will be adequate for most asbestos-processing locations. Rubble breakers will need a larger capacity, probably 5000 $m^3.h^{-1}$. The capacity required in production plants will largely depend on the production volume.
In incinerators, the measures will involve improvement of the electrostatic precipitators. The capital outlay (for 11 incinerators) is f 81 million and the operating costs are f 17.5 million per year.

Concentration of activities

Concentration of activities will be aimed specifically at activities which are too small-scale for cost-effective implementation of emission-control measures, such as maintenance work on brakes and (pre)treatment of asbestos cement. The cost factors involved in this type of measure are:

- transport costs to and from central "facilities"
- enlarging the capacity of chosen/designated "facilities"

- loss of working hours resulting from not making size corrections on site in asbestos cement processing, as well as from working less efficiently because of the need to service vehicles at two locations.

The cost of these measures will have to counterbalance the cost of installing various small exhaust and air purification units, so that the maximum costs will not exceed those for installing these units. An accurate cost estimate for this measure cannot be made.

Containment of asbestos

The cost of containment at the site where the asbestos-containing material has already been installed is largely determined by labour costs and is consequently heavily dependent on how accessible the material is. The following approximate costs have been assumed:

- impregnation: f 75.- to f 100.- per m^2 (this usually requires working in difficult positions and wearing protective clothing)
- double walls, ceilings, etc.: f 125.- to f 175.- per m^2 (the cost of materials is an important consideration here.

It is much cheaper to treat new asbestos cement in the factory. The material used constitutes the major expense item, viz. f 2.50 to f 3.- per m^2, and increases the cost price of asbestos cement by about 10-20%.

Modified work practices and processing techniques

In the production of asbestos-containing materials, far-reaching measures will usually be taken where modification and modernization have already been planned. It is not possible to determine accurately how much emission control will cost in this process- integrated approach.

Modified dust-suppressing equipment for processing asbestos cement is not always much more expensive. In some instances, cheaper equipment appears to perform even better in this respect. It has been reported in the literature that the present generation of low-dust processing equipment has been improved in terms of practicability and can compete with the "regular" equipment (Teichert, 1983). There are a total of several hundred machines in the Netherlands, with prices ranging from f 100.- to several thousand guilders.

The cost of modifying operating practices (good housekeeping) is difficult to quantify, because wages account for nearly 100% of this. Special attention, but no extra time, is sometimes all that is needed. However, assuming that extra time is required before demolition can be undertaken,

then this is estimated to cost f 30.- to f 50.- per m^2, or f 3.- to f 4.- per kg.
Measures required to limit emissions as far as possible in the removal of sprayed asbestos are of the order of f 100.- to f 150.- per m^2. These costs are heavily dependent on the method used for applying the asbestos (loose or glued) and on whether extensive scaffolding is necessary.

7.7. SUMMARY AND CONCLUSIONS

Extensive measures to reduce asbestos emissions have been taken in the production of asbestos cement and brake linings, the principal applications remaining in the Netherlands. Materials to replace asbestos in these applications are available. A breakthrough to complete substitution of asbestos cement is not yet to be expected. Partial substitution of asbestos-containing braking materials has already taken place, but complete replacement in the short term does not appear likely at present. Accumulated asbestos in durable products, mainly buildings, remains an important source of large, but very diffuse, emissions. These emissions, particularly those into soil and air, will even increase in the coming years because of renovation and demolition of buildings.
In the processing of asbestos-containing waste streams, the aim is concentration and controlled transport to disposal sites, whereby only minimal emissions into water and air are permitted. For the dumping of concentrated asbestos waste consisting of practically unbound asbestos such as sprayed insulation (500 tonnes per year), in particular, extensive measures have been taken. Immobilization of this "free-form" asbestos will cost about f 100,000.- annually, and there will also be a comparable increase in the dumping charges. Controlled processing of waste streams in which asbestos is strongly diluted is almost impossible.
The remaining possible measures, aimed at preventing dust from becoming airborne during dumping and rubble breaking (for reuse), are mostly already being implemented.
Asbestos emissions into water caused by the discharging of waste water from a variety of production processes have all but ceased, because the relevant products are no longer manufactured, or because measures, such as recirculation of process water, have been taken. The sole large localized emission source remaining is the replacement of asbestos-based electrolysis diaphragms. To reduce this, effective waste water treatment is necessary

but expensive. The most important diffuse emission is the result of the weathering and wearing of asbestos-containing materials such as corrugated roofs. Here, emission control must be effected through substitution by asbestos-free materials.

The largest cuts in asbestos emissions into the air are obtained by changing to asbestos-free materials. In addition, new products (e.g. corrugated sheet roofs) could be coated with a protective layer. In locations where asbestos-containing products are processed or replaced, resulting in the release of asbestos fibres (brake maintenance, sawing to size of asbestos cement, etc.), space exhaust must be provided where posssible. Such activities could be concentrated in a number of locations where emission-control measures can be implemented.

A summary of the measures and costs for the principal emissions is given in table 7.3.

Table 7.3. Measures to reduce the principal asbestos emissions into air

Emission	Emission (in 1982)	Estimated reduction	Estimated residual emission	Measures[1]					Costs per year	Costs per kg
	(kg/year)	(%)	(kg/year)	S	Ex+ECT	C	Co	MWP	(mln f)	(1000 f)
- Brake dust on roads	600	90	60	(+)					not known	
- Production of braking and friction materials	300	99	3	(+)	+[6])				0.37	1.2
- Demolition of buildings	200	90	20[4])					+	5.5	30
- Brake dust in garages	365	99	3.6	(+)	+	+		(+)	56	227
- Rubble breakers	80	99	8		+				3.9	55
- Processing of asbestos cement on site	445	99	4.5	(+)	+	+		(+)	1.5	28
- Processing of insulation, packings, etc.	54	90	5	(+)				+	not known	
- Demolition/replacement of insulation, packings, etc.	54	90	5					+	not known	
- Household waste incineration	50	90[5])	5		+[2])				17.5	390
- Dumping of waste	45	-	45				+[6])	+[6])	not known	
- Production of insulation, packings, etc.	20	-	-	+[3])					-	-

[1]) Applicable measures:
S = Substitution of asbestos by an alternative
E+ECT = Exhaust and emission-control technique
S = Substitution of asbestos by an alternative
C = Concentration of activities makes possible effective exhaust and application of ECT
Co = containment
MWP = Modified work practices
The measures in brackets are theoretically possible

[2]) improved emission reduction
[3]) production has ceased
[4]) note that the asbestos content of the structures to be demolished increases (se section 7.2.)
[5]) improvement of electrostatic precipitators from on average 95% (in 1982) to 99.5%
[6]) already implemented

Finally, it should be noted that an estimate of the costs for alternatives and emission control can be readily made in the case of highly localized sources. However, the largest emissions into air and water usually arise from diffuse sources, for which the cost of measures is much more difficult to determine.

8. FINANCIAL CONSEQUENCES OF EMISSION REDUCTION

The (costly) replacement of asbestos cement sheets and packing materials (section 7.3.) and measures designed to counteract further weathering (subsections 7.5.1. and 7.6.1.) affect both companies and households. Allocation of the costs to particular industrial sectors is in fact impossible, and the same is true of extra provisions in the demolition of buildings and insulation. The cost of additional treatment of flue gases from domestic waste incinerators can be passed on to the households. This will not be discussed here.

Industries for which specific measures are being proposed are asbestos cement-processing plants and garages. Any financial consequences will have the greatest impact on these sectors. Incidentally, these measures need not be implemented if asbestos in brake linings and building sheets is replaced by alternative materials within a few years. Replacement of asbestos cement sheet may have adverse consequences for the Dutch producer. Since all the packing material is imported, compulsory substitution will pose fewer problems here.

This chapter will consider the financial consequences of the proposed measures for the asbestos cement products industry, the wholesale trade in building materials, and the garages (car repair shops). An outline is given of the nature, size and composition of each industrial sector (structural outline). The MIOW method ('t Gilde et al., 1986) has been used to gain an insight into the functioning of each sector. This method distinguishes three key variables: market situation, international competition, and staying power. The value of the key variables is determined on the basis of a number of distinctive features of each industrial sector. The three variables, considered in connection with one another, characterize the situation in which the particular industrial sector finds itself. This situation determines the leeway which companies have in reacting to externally imposed measures. By setting this leeway alongside the environmental cost estimated in chapter 7, an attempt is made, for each industrial sector, to arrive at a prediction of how the entrepreneurs will react to the proposed measures.

8.1. ASBESTOS CEMENT PRODUCTS INDUSTRY

Structural outline

There is only one company in the Netherlands which manufactures asbestos cement products. Only an overall picture can be given because of the confidentiality of the figures. The firm had a turnover of f 90 million in 1984 and employed 300 people (220 fewer than in 1981).

Market situation

The company manufactures building materials. The three principal products are:

- corrugated sheet for agricultural utility buildings
- flat sheet employed as external and interior wall cladding
- pipes for drinking water supplies and sewerage

Flat sheeting is increasingly being supplied in the asbestos-free version. The ratio of the relative importance of pipes to that of sheets is roughly 1:2.

As a result of the decline in building activities after 1982, the market for pipes, which relies entirely on government investments, has approximately halved. Both residential and non-residential construction have fallen by about 30%, while until 1985 the market for agricultural utility buildings declined by some 20%. The prospects for the agricultural sector do not look promising for the coming years, because the measures designed to curb the milk and manure surpluses will lead to a decrease in building investments in the long run. The market for the other sectors is assumed to stabilize.

The market share has remained static over the past few years. The firm strives to maintain or enlarge its market share, but meets with strong price competition. In the pipe market, there is stiff competition with (asbestos-free) concrete pipes and PVC pipes. Since a corrugated-sheet roof is about 30% cheaper than traditional roofing, the firm's competitiveness in this market is strong.

International competition

The import and export of building materials are relatively small. The concrete products industry, for example, which has a strong affinity with the asbestos cement products industry, exports 7% of its production. The export share of the manufacturer of asbestos cement products is 14%. This

seemingly high percentage is due to the restructuring which took place in 1982, with the plant in the Netherlands now specializing in the production of sheets and the Belgian plant in pipes. Thereafter, an export flow of sheets and an import flow of pipes developed, which actually involves intra-concern deliveries. Only a few per cent constitute "real" exports to West Germany. The importation of corrugated sheets is considerable: 60% of the corrugated sheets used in the Netherlands come from abroad.

Staying power

The operating results in 1984 amounted to 4% of the turnover and total capital. The net profit in that year was 4% of turnover, or 7% of ownership capital, which is low.

The company's solvency is good. Ownership capital accounts for 60% of the total. Since no insight could be gained into the financial structure of the concern as a whole, this figure should be viewed with some caution.

The cost makeup is insufficiently known to be able to give a full breakdown. Labour costs account for 25% and depreciation for 5% of the production costs. These figures suggest a labour-intensive and moderately capital-intensive enterprise. The concrete and cement products industry as a whole is known to be not very energy-intensive, and there are no reasons for assuming that this would be otherwise for this firm. The company has invested some tens of millions of guilders in environmental provisions in the form of exhaust systems and cloth filters.

8.2. WHOLESALE TRADE IN BUILDING MATERIALS

Structural outline

The wholesale trade in building materials functions as a link between the producers of building materials on the one hand, and building contractors and do-it-yourselfers on the other. Operations such as sawing and drilling are carried out to a limited extent, as requested by contractors.

In the Netherlands, this industrial sector comprised 2047 businesses at the end of 1983, which is 3% fewer than in 1980. There are many small enterprises: about two-thirds employ fewer than 10 persons. Of all wholesalers, 106 have specialized in the sale of sheet material, and these are on average slightly larger: about half employ fewer than 10 persons.

Turnover was f 11.9 billion in 1984, up 5% on 1982, but still 13% lower than in 1980 (1980 sales: f 13.9 billion). These figures reflect the severe

decline which took place in the construction industry after 1980. The wholesalers specializing in sheet material achieved a turnover of f 1.4 billion in 1984. This sector, too, was confronted with a falling demand after 1980, but the decline was slightly less than the average: 5% between 1980 and 1984.
In 1982, about 24,000 people worked in the wholesale trade in building materials. This number fell by 20% between 1980 and 1982, and this downward trend continued, albeit less rapidly, between 1982 and 1984, namely by 10%. The small businesses (two-thirds of the total) account for 25% of turnover and employment. The other 75% are concentrated in 600 medium-sized enterprises. In 1982, over 2100 people worked in the sector specializing in sheet material, about 25% of these likewise in small businesses.

Market situation

The wholesale trade in building materials is heavily dependent on the situation in the construction market, which was unfavourable between 1980 and 1983, and no improvement is envisaged before 1990 (CPB, 1986). In the coming years, market saturation is expected to continue.
Dutch customers account for 95% of sales. The market share is stable and therefore did not play a part in the downturn in trading. Clear economies of scale do not exist within this industrial sector, and both margins and cost makeup are broadly the same for the small and the medium-sized business. Consequently, both groups of businesses were equally hard hit by the unfavourable market situation.
Competition has been stiff in recent years because of the shrinking market. Since the price was wielded as the largest weapon, earnings and margins came under added pressure. Although the pressure has now eased, price competition continues to set the scene. Competition occurs for the most part in regional markets.

International competition

The regional market is the relevant outlet for building materials; exports are consequently insignificant, namely 5%. The export figure is even lower for the businesses specializing in sheet material: 2%. International competition does not therefore play an important part.

Staying power

Profitability has been very low or negative over the past few years, particularly for the businesses specializing in sheet material. The situation in 1984 had improved insofar that losses were no longer recorded. The results were still very low, namely, about 1% of the turnover, or about 2% of the total capital.

Ownership capital represents 20% to 30% of the balance sheet total, which is satisfactory within the wholesale trade generally. Supplier's credit plays an important part in the financing of the wholesale trade, providing 26% of the capital required.

Sales margins for the wholesale trade in building materials are on average 21%. About half of the margin is spent on labour costs, including entrepreneurial renumeration. Depreciation expenses use up 9% of the margins (2% of turnover). All in all, this industrial sector is moderately labour-intensive and not particularly capital-intensive.

8.3. GARAGES (CAR REPAIR SHOPS)

If the substitution of asbestos-containing braking material fails to materialize, emission-reduction measures will be necessary, certainly in the light of the outlined autonomous development in the asbestos emission from maintenance work in the garages. The financial consequences of such measures are examined here.

Structural outline

This industrial sector comprised 8414 businesses in 1984, 7% fewer than in 1980. The number of businesses has remained the same since 1983. Small businesses are in the majority: 87% have fewer than 10 employees, the average being 7 persons. Two-thirds are one-man enterprises.

The garages produced a turnover of f 23.6 billion in 1985, up 10% on 1984, including an 8% increase in volume. Sales, after adjustment for inflation, appear to have changed very little between 1980 and 1985.

The stagnating sales during the years 1980-1983 led to falling employment in this sector. The number of employees decreased by 16%, from 64,400 to just over 54,100, of whom 50% were employed in the workshops. Thirty per cent of the businesses concentrate mainly on the sale of cars and 70% on maintenance work. The latter group accounted for 86% of the turnover of the garages in 1982.

Market situation

Garages are active on the car-sale and maintenance markets. Automobile dealers account for the greater part (65%) of the turnover.

The number of new cars sold fell after 1979, but has grown again since 1984 and is expected to stabilize in the coming years (BOVAG, 1987). Because of low margins (4% to 10%), the contribution of selling activities to the value added and employment is relatively small. Maintenance and repair account for a much smaller proportion (17%) of the turnover, but because of the margin of 33%, as well as the high labour intensiveness, their contribution to the value added and employment is relatively large. Sales did not grow despite the increase in car ownership and mileage, because new car types require less servicing. The servicing time per car fell between 1981 and 1986 from 8.5 to 6 hours a year, a decrease of about 30% (EIM, 1987). The postponement of maintenance, as a result of the bad economic situation, also contributed to this. The introduction of the periodical M.O.T. test leads again to more regular checks and servicing. On balance, the maintenance market is expected to decline slightly (BOVAG, 1987). Because of the labour-intensive nature of maintenance repair, it is financially attractive for the car owner to do this work himself ("do-it-yourself") or have it done informally ("moonlighting"). Consequently, only half the parts are fitted by the garages. Cars are preferably taken to garages not too far away from home for maintenance: it is a regional market. Small businesses do not fare better or worse in these markets than medium-sized or large enterprises.

The main features of the maintenance market are keen price competition and high price sensitivity within a mature, somewhat declining market.

International competition

Competition with foreign businesses will only play a part in the regions near the borders. Practically speaking, therefore, Dutch garages control nearly 100 per cent of the Dutch market, so that international competition is practically nonexistent.

Staying power

The profitability of the garages is low. The results for the sector as a whole are about 3% of the turnover. When deducting the renumeration for owners of one-man businesses from this, average profits are close to zero. The net profit of the garages was 0.4% of turnover in the bad years

1982/83, and 0.9% in 1985. Further improvement is not very likely in the coming years (EIM, 1987). The maintenance activities are often loss-making, which must be compensated for by profits on the sale of cars (NMB, 1986). There is very little difference in the profitability of small and medium-sized enterprises. The solvency of the garages fluctuates between 17% and 28%, which is considered normal within the retail trade and service sector. The variable costs (chiefly the parts used) account for 67% of maintenance and repair costs. Labour costs, including the entrepreneurial renumeration, take up two-thirds of the sales margin of 33%. Depreciation expenses account for 6% of the margins, or 2% of the cost price. The garages are moderately labour-intensive and not very capital-intensive.
The garages invested f 391 million in 1984. Their staying power must be regarded as weak, which is especially due to their low profitability. It is inescapable that some garages will disappear (EIM, 1987).

8.4. SUMMARY AND CONCLUSIONS

Table 8.1. summarizes the most important data on the industrial sectors discussed. For each sector, the increase in costs resulting from the measures described in chapter 7 is indicated. This is not possible for the asbestos cement products industry, because this sector is confronted not so much with emission-control measures as with a possible asbestos ban on (corrugated) sheets.

Table 8.1. Characterization of a few industrial sectors and the increase in costs resulting from possible emission-reduction measures

Sector	*Structure (business size)*	*Market situation*	*International competition*	*Staying power*	*Increase in costs (% of value added)*
Asbestos cement products	*medium-size*	*fair*	*moderate*	*fair*	*n.a.*
Wholesale trade in building materials	*small*	*weak*	*little*	*weak*	*0.5%*
Garages	*small*	*weak*	*little*	*weak*	*4.2%*

The asbestos cement products industry in the Netherlands consists of one medium-sized company with reasonable staying power. The constituent markets operate under somewhat diametrically opposed circumstances: the pipe market is weak but faces little international competition, whereas the corrugated sheet market is reasonably strong but has to compete with a large volume of imports. A possible asbestos ban would clearly have an adverse effect on

competitiveness. Although the company concerned can and would do much to adjust to the new situation, a fall in sales and thereby in employment seems likely.

The wholesale trade in building materials is a small-scale industrial sector. Both the market situation and staying power are weak, but international competition is insignificant, which makes it easier to pass on increases in cost to the customer. For the wholesale trade in sheet material, the environmental costs of exhaust and filtration provisions constitute 0.1% of the turnover and 0.05% of the margins (which can be equated to the value added). This means a small additional burden, which will be relatively heavier for the many small businesses in view of the indivisibility of the investment. The proposed measures will not have major consequences for the sector as a whole, although small businesses may run into difficulties.

The garage sector comprises a group of small-scale businesses, with a weak market situation and weak staying power. On the other hand, international competition hardly affects them. If each garage must be able to continue carrying out brake maintenance, the environmental costs for exhaust and filtration provisions, related to the maintenance activities, will constitute 1.4% of the turnover and 4.2% of the margins; a considerable increase in the financial burden. The required total capital outlay of f104 million amounts to 26% of the total annual investments by the garages; a high percentage. Small businesses will be harder hit by the extra costs because of the indivisibility of the investment to be made. Assuming that half the expenditure can be passed on to the customers, the measures will lead to a noticeable deterioration in the financial position. The disappearance of small enterprises, in particular, and a slight fall in employment, is then likely. This effect strengthens the tendency already present to reorganize this industrial sector.

9. EVALUATION

9.1. RISKS AND RISK GROUPS

9.1.1. Risks to man

The principal effect of asbestos on man is the development of cancer. With respect to oral exposure, the available studies do not suggest that asbestos is carcinogenic. Although there is insufficient knowledge about the occurrence of asbestos in food and drinking water, it is assumed that the current load via ingestion poses a negligible risk.

Animal studies as well as observations in humans have furnished sufficient evidence that asbestos causes lung cancer (bronchial carcinomas) and cancer of the pleura and peritoneum (mesotheliomas) following inhalation. The carcinogenic potency of asbestos appears to be mainly a function of fibre dimensions (length and diameter). As regards the induction of mesotheliomas, the durability of the fibres in the tissues is also relevant. In this connection, chrysotile asbestos is less potent than amphibole asbestos. Fibres with a length of 20 μm or more and a diameter of 0.1-0.25 μm have very likely the highest relative carcinogenic potency, which decreases with decreasing length and/or increasing diameter of the fibres. Strictly speaking, "safe" fibre dimensions within the limits of the respirable fraction (< 200 μm long and 3 μm in diameter) cannot be given. The risk from fibres shorter than 5 μm, which in theory could still possess some carcinogenic potency, will be negligible in practice, and these will therefore not be considered in the risk evaluation.

The risk of developing lung cancer (latency period is about 10 years) is approximately linearly related to the duration and intensity of exposure. The risk of mesotheliomas is linearly related to the intensity of exposure but exponentially related to the time from onset of exposure. Concerning the calculation of the excess risk for mesotheliomas and lung cancer from lifetime exposure to a certain asbestos concentration, the following comments are made:

- The quantitative risk evaluation is based on epidemiological data from occupationally exposed humans. However, exposure levels in work situations were usually not directly measured but estimated. This method is very inaccurate for asbestos fibres. Any quantitative extrapolation

from work situations to much lower exposure levels can therefore give no more than a rough indication of the risks.

- The risk of lung cancer is about ten times higher for smokers than for non-smokers, and is multiplicative to the risk from asbestos exposure. The risk of mesotheliomas is not influenced by smoking. The risk ranges for lung cancer given in this document are however so wide that they encompass the risks to both smokers and non-smokers. For this reason, it is not realistic to calculate a separate risk figure for smokers and non-smokers. The figures given apply to an average population with an estimated 30% smokers.
- The calculation of the risk from occupational situations is based on optically visible fibres (detection limit: length > 5 μm; diameter > 0.3 μm). Results of ambient air measurements in the Netherlands show that the median fibre diameter lies within a narrow range around the value of 0.1 μm, so that environmental fibre concentrations have to be measured by electron microscopy. A factor of 2 is generally used as a conversion factor which must be applied to make possible extrapolation of the risks from occupational situations to those for ambient air (2 EM fibres = 1 LM fibre). This factor would be higher if the current ambient air concentrations were measured with light microscopic methods (for example, a factor of 10), because ambient air contains relatively more fibres with dimensions below the detection limit of the light microscope. This method cannot therefore be recommended.

In summary, it can be stated that the asbestos present in the ambient air must be determined as fibres (= particles with a length/diameter ratio of 3:1 or more), longer than 5 μm, per m^3, by electron microscopy. A distinction should be made here between chrysotile and amphibole fibres.
The estimated approximate risks to the general population, for lifetime exposure to asbestos measured as described above, are given in table 9.1.
The table shows that exposure to amphiboles is associated especially with an excess of lung cancer, whereas chrysotile causes mainly an increased risk of developing lung cancer.

Table 9.1. Estimates of the lifetime risk to the general population, for lifelong exposure to asbestos in the ambient air

Effect	*Lifetime risk **	*Fibres > 5 μm per m³, measured by electron microscopy*
Mesotheliomas	10^{-6}	*10- 100 (amphiboles)*
(for smokers and		*100- 10,000 (chrysotile)*
non-smokers)	10^{-4}	*1,000- 10,000 (amphiboles)*
		10,000-100,000 (chrysotile)
Lung cancer (for a population	10^{-6}	*100- 1,000 (chrysotile)*
with 30% smokers)	10^{-4}	*10,000-100,000 (chrysotile)*

* *The standardization policy (IMP-Environmental Management 1986-1990) considers a lifetime risk of 10^{-6}, corresponding to approximately 10^{-8} per year, to be the "negligibility level". This policy considers a lifetime risk of 10^{-4}, corresponding to approximately 10^{-6} per year, to be the maximum allowable risk.*

An estimate of the exposure of the general population in the Netherlands to asbestos, excluding exposure in public buildings where sprayed asbestos has been applied, is given in table 9.2.
This estimate was derived from the total fibre concentration as measured by EM (see section 5.6.), assuming that 10% of the total number of fibres in the ambient air is longer than 5 μm. For the immediate vicinity of sources, this assumption may lead to underestimation of the risk, because it is especially in these areas where the highest percentage of long fibres is found. Since amphibole fibres were found in measurable quantities in the ambient air at only one location in the Netherlands, the quantitative risk evaluation is based on exposure to chrysotile.

Table 9.2. Estimates of asbestos exposure levels of the general population in the Netherlands, expressed in numbers of fibres, longer than 5 μm, per m³, determined by electron microscopy

Residential area	*Exposure level*
Rural areas, medium-sized towns	*10- 100*
Large towns, industrial areas	*30- 325*
Immediate vicinity of sources	*255-2575*

Comparison of the estimated exposure levels (table 9.2.) with the risk estimates (table 9.1.) shows that the expected lifetime risk of lung cancer in the immediate vicinity of sources is higher than 10^{-6}. In the large towns and industrial areas, this risk falls within the ranges indicated, although a risk can also here not be excluded in all cases because the upper limit of the exposure levels measured is much higher than the lower limit of the levels associated with a lifetime risk of 10^{-6}. The expected lifetime risk of mesotheliomas from exposure to amphiboles, as measured at

one location in the Netherlands, is also higher than 10^{-6}, while that from exposure to chrysotile, as observed in the ambient air, appears to be negligible (lower than 10^{-6}. The expected lung cancer and mesothelioma risks for lifetime exposure via outdoor air remain everywhere in the Netherlands below the value of 10^{-4} (10^{-6} per year) which the standardization policy (as laid down in the IMP-Environmental Management 1986-1990) considers to be the maximum allowable risk. Risk groups which may be exposed to high asbestos levels are (in addition to the workers in the asbestos-producing and -processing industries) persons who, by virtue of their profession, spend long periods of time in public buildings and offices where sprayed asbestos has been applied, and demolition workers.
Furthermore, heavy physical exertion increases the respiration rate and thereby the exposure dose. Smokers constitute a risk group with an increased susceptibility to lung cancer.
Finally, it should be noted that the biological activity of asbestos appears to depend largely on the fibre dimensions, so that it is not inconceivable that substitute materials, with comparable characteristics and physical properties, may have a similar biological effect to asbestos. This should be taken into account when introducing alternatives for asbestos on a large scale.

9.1.2. Other risks

Few data are available on the effects of asbestos on ecosystems. In view of the individual approach concerning the risks to man, the risks to ecosystems and their constituent parts are as yet regarded as being non-critical. The possible effects of asbestos on materials and on a global scale are considered to be of minor or no importance.

9.2. FEASIBILITY OF RECOMMENDED VALUES

At present, there are no quality requirements in the Netherlands for asbestos in the general environment.
Chapter 3 shows that asbestos fibres, because of their relative inertness, remain in the environment for an appreciable time: fibres can begin to participate in a cycle, consisting of deposition and resuspension, whereby the wind conditions, the relative humidity and mechanical activity

determine how many fibres end up in the air. This implies that the large-scale concentrations will be largely determined by re-emissions. The magnitude of these re-emissions in the future is the resultant of the development of the emission levels and the withdrawal of asbestos from the cycle by emission-control measures and wet deposition (the natural degradation of asbestos is here considered to be negligible). As has already been mentioned, the large-scale concentration results in exposure levels at which the anticipated risks are not negligible in all cases, although in terms of policy (IMP-Environmental Management), there are no unallowably high risks as yet. When the asbestos emission is larger than the amount of asbestos which is withdrawn from the cycle, higher exposure levels may, however, be expected in the long term, with correspondingly higher risks. This will be the case with an autonomous development. The contribution of emissions arising during the production and processing of asbestos is now very limited because the number of asbestos applications has fallen drastically since the early 1980s. However, an increase in the emissions is expected, especially because of the larger amount of asbestos which will be set free during demolition and renovation activities (table 7.1.: an approximately threefold increase in the period 1985-2000). This emission can be reduced by some 90% by modifying the work procedure; the cost amounts to about f 5500 per year, i.e., about f 30 per kg of asbestos emission avoided. The other important emissions into air (brake dust on roads, production of braking and friction materials, and brake dust in garages) will probably also increase because these emissions are to a considerable extent linked to the growth in road traffic. Stimulation of the use of substitute materials seems desirable here. However, it should be borne in mind that some alternative materials may have a similar biological effect to asbestos; this should be evaluated for each material and application area.

Although the measures outlined appear to be adequate to prevent the unallowably high risks in the future, as defined from policy (IMP-Environmental Management), insufficient insight exists into the contribution of emission versus re-emission, the contribution of the Netherlands versus foreign countries, and in the magnitude of natural withdrawal from the cycle, to make a statement about the development of the large-scale concentration.

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APPENDIX TO CHAPTER 6

ESTIMATE OF THE LUNG CANCER AND MESOTHELIOMA RISKS AFTER LIFETIME EXPOSURE TO ASBESTOS

1. Calculation of mesothelioma risk by the WHO working group for Air Quality Guidelines (1987)

Estimates of the mesothelioma risk by various authors, as given in table I.1., were made on the basis of data on exposure and effects in a small number of occupationally (predominantly amphiboles) exposed cohorts, using the following formula:

$$I_M = f \times (t-w)^k$$

where I_M = the mesothelioma incidence, f= fibre exposure dosage, t = years since first exposure, w = latency period in years (usually 10), and k = an empirical constant (2 to 3.5)

The values obtained for the lifetime risk varied from 0.2 to 2.4 per 10^5 inhabitants for lifelong exposure to 100 f* (= optically visible fibres; see table I.1.) per m^3, which corresponds to 10^{-5} to 10^{-4} for lifelong exposure to 500 optically visible fibres per m^3 (= 1000 fibres.m^3 as measured by electron microscopy).

Table I.1. Estimates of the lifetime risk of mesothelioma after lifelong exposure to asbestos, by various authors, as reported in the WHO Air Quality Guidelines (1987)

Author	*Values as given in original publication*	*Mesothelioma risk calculated by WHO working group per 10^5 for f*.m^{-3}*
Federal Health Office, FRG, 1981	*$10/10^5$ for 100 f*.m^{-3}*	*1.0*
Schneidermann et al., 1981	*$10/10^5$ for (130-800) f*.m^{-3}*	*ca.2.0*
NRC, 1984	*$9/10^6$ for 400 f*.m^{-3}*	*ca.2.0*
EPA, 1985	*$275/10^5$ (F) for 0.01 f.ml^{-1}*	*ca.2.4*
	$192/10^5$ (M) for 0.01 f.ml^{-1}	

f = fibres measured by optical microscopy, corresponding to 2f (fibres longer than 5 μm, measured by electron microscopy)*

2. Calculation of lung cancer risk by the WHO working group for Air Quality Guidelines (1987)

The lung cancer risk for lifetime exposure to asbestos can be represented by the following formula:

$$I_L = I_L^o \times (1 + K_L \times f \times d)$$

where I_L is the lung cancer incidence after exposure to f x d fibre years (f-y) asbestos, and I_L^o is the lung cancer incidence without asbestos exposure

The factor K_L in this formula can be calculated using data on exposure and effects in different occupationally asbestos exposed cohorts, as was done by Liddell and Hanley (1985), among others (see table I.2.).

The calculated K_L varies between 0.04 and 1.6 per 100 f*-y.ml^{-1}, i.e. 0.0004-0.016 per f*-y.ml^{-1}(the highest value of 2.7 per 100 f-y.ml^{-1} for women was not included). For comparison: the EPA found values for K_L ranging from 0.0001 to 0.07 per f-y.ml^{-1} (EPA, 1985).

Table I.2. Estimates of the increase in lung cancer incidence, K_L, in various studies, according to Liddell and Hanley (1985), as reported in the working document of the WHO Air Quality Guidelines (1987)

Risk K_L per 100 f-y.ml^{-1}	*Type of industry*	*Reference*
0.04	*mining, milling*	*McDonald et al., 1980*
0.045	*mining, milling*	*Nicholson, 1979*
0.06	*friction materials*	*Berry and Newhouse, 1983*
0.1	*manufacturing processes*	*Henderson and Enterline, 1979* *Enterline et al., 1972*
0.4-1.1 (M)	*manufacturing processes*	*Newhouse and Berry, 1979*
2.7 (F)	*manufacturing processes*	*Newhouse and Berry, 1979*
0.2	*asbestos cement*	*Weill et al., 1979*
0.07	*textile (before 1950)*	*Peto, 1980*
0.8	*textile (after 1950)*	*Peto, 1980*
1.6	*textile*	*Dement et al., 1982*
1.6	*textile*	*Fry et al., 1982*
1.1	*insulation products*	*Seidman et al., 1979*
1.5	*insulation products*	*Selikoff et al., 1979*

In the first instance, the WHO working group calculated, using the K_L values of Liddell and Hanley (1985), the excess risk of lung cancer for lifetime exposure to 100 $f^*.m^{-3}$, by assuming:

- The lung cancer risk in the absence of exposure to asbestos is 10% for smokers, and 1% for non-smokers.
- Lifetime exposure is approximately equal to 50 years (the first 20 years were ignored because of non-smoking).
- For extrapolation of data from occupational situations (exposure during 0.24% of the life-span) to the general population, the length of time was multiplied by a factor of 4.

Substitution of these data in the formula gives (lowest K_L value):

$$I_L = 0.1 \text{ (= lung cancer risk smokers)} \times (1 + 0.0004 \text{ (= } K_L \text{ per f-y.ml}^{-1}\text{)} \times 0.0001 \text{ (= concentration in f*.ml}^{-1}\text{)} \times 4 \text{ (= correction factor)} \times 50 \text{ (= years of exposure)}$$

$$= 0.1 \times (1 + 8\times10^{-6})$$

The excess risk of lung cancer is then $I_L - I_L^o = 0.1\times(1 + 8\times10^{-6}) - 0.1 = 8\times10^{-7}$ for smokers, and 8×10^{-8} for non-smokers.
For the highest K_L value, the excess risk is calculated at $0.08\text{-}3.2\times10^{-5}$ for smokers, and (10 x lower) $0.08\text{-}3.2\times10^{-6}$ for non-smokers, for lifetime exposure to 100 $f^*.m^{-3}$.

Subsequently, it was concluded that such a risk calculation suggested an accuracy which did not exist, and orders of magnitude were given instead of single figures.
For lifelong exposure to 500 $f^*.m^{-3}$ (= 1000 $f.m^{-3}$), the risk calculated according to the above formula would be $0.4\text{-}15\times10^{-5}$ for smokers, which corresponds to a lifetime risk of approximately 1×10^{-6} - 5×10^{-5} for a population with 30% smokers.
The order of magnitude finally given, 10^{-6} to 10^{-5} for a population with 30% smokers, was partly based on risk estimates made by others (WHO Air quality Guidelines, 1987).

3. Calculation of mesothelioma risk in this integrated criteria document

With respect to exposure to amphibole asbestos, the risk assessment of the WHO has been adopted. For chrysotile, however, the assessment of Doll and Peto (1985) has been used, who arrived at an approximately 20 times lower mesothelioma risk after exposure to chrysotile than to amphiboles. This risk would then be approximately $5x10^{-7}$ to $5x10^{-6}$ for lifelong exposure to the same fibre concentration.
A lifetime risk of 10^{-6} for mesotheliomas will thus be caused by exposure to about 5-50 amphibole fibres or 50-5000 chrysotile fibres per m^3 as measured by OM in occupational situations, which is roughly equal to 10-100 and 100-10,000 fibres, longer than 5 μm, per m^3 respectively, as measured by EM in ambient air.

4. Calculation of lung cancer risk in this integrated criteria document

The risk assessment of the WHO for lung cancer has been adopted. Assuming a risk of 10^{-6} to 10^{-5} for lifetime exposure to 500 $f^*.m^{-3}$, it can be calculated that a risk of 10^{-6} will be caused by lifetime exposure to 50 to 500 asbestos fibres (all types), longer than 5 μm, per m^{-3}, as measured by EM in ambient air.

ADDENDUM INDUSTRY

1. GENERAL

The document contains a wealth of information, which in a number of respects gives a good selection of the extensive literature that exists on the relationship between asbestos and human health. Unfortunately, there are passages in the text which do not completely agree in their conclusions.
It is stated about chrysotile in the assessment of the mesothelioma risk that this asbestos type is 20 times less hazardous than amphiboles.
In the summary it is stated that chrysotile seems to be less hazardous. In fact, it concerns here a conclusion of vital importance with respect to the biological effects of chrysotile.
Such ambiguity should not occur in a document which serves as a scientific basis for the formulation of the effect-directed standardization policy.

It is furthermore mentioned in the document that chrysotile is the only asbestos type used in the Netherlands since 1978, and which measurements have shown to be present in the air (except at one location; see below).
All aspects discussed should therefore have concerned this variety. However, a large number of studies are mentioned in which the asbestos type involved is not specified at all. For example, the studies by Selikoff, referred to several times, were conducted among insulation workers who predominantly worked with non-locked-in amphiboles, and these therefore make any transposition to the environmental situation in the Netherlands irrelevant.

2. SPECIFIC

2.1. Emission calculation

Although it is mentioned that, from a medical viewpoint, only the fibres with a length of > 5 μm and a diameter of < 3 μm are important, different quantities are alternately used in the document.
Emissions are always expressed in kilograms or tonnes, but it is not stated what proportion of this is medically relevant.

A large fraction of the fibres is already shorter than 5 μm, and can therefore never again assume the biologically active dimensions.
The various emission sources emit fibres of widely different dimensions. Coarse particles are often also emitted, which are not respirable and will settle rapidly.
The emission data used in the document are based on old literature. Assumptions have been made which subsequently appeared to be incorrect. Furthermore, methods are used which have meanwhile been considerably improved.
The emissions into the air are grossly overestimated, the processing of asbestos cement on site being an example of this. It is supposed on page 20 that 1 kg of dust with about 10% asbestos is emitted per tonne of asbestos cement processed. It is stated on page 44 that the emitted asbestos contains 2,000-40,000 fibres per kg. This implies that during the manipulation of one 25-kg corrugated sheet 5×10^{12} fibres would be released within some tens of seconds. Even if only 1% of these fibres were included in the optical microscopic count, it is clear that the MAC value would be exceeded in this operation by several orders of magnitude (see subsection 5.4.1.). A similar approach can be adopted for rubble breaking, building demolition and the dumping of asbestos cement waste.
It is obvious that two different concepts of emission are used in this report: one pertaining to coarse particles with a short residence time in the air, and one to fine particles which remain airborne for a long time.
In our opinion, the first type, consisting of particles falling between the point of origin and the ground, should not be regarded as emission.
The data on emissions into the air are consequently overestimated by several orders of magnitude. The emissions marked with ** in table 2.14. (page 34). should be omitted. The conclusion that emissions will increase considerably in the future is therefore incorrect. The sources which are supposed to increase substantially are much less important than the document states.
Other inaccuracies leading to overestimation of the asbestos dust released into the air are:

- The estimate that, by 2030, the asbestos cement freed during demolition will be twice the current annual consumption. We do not believe in an accelerated demolition.

- The wearing of felt-backed floor covering produces PVC as waste and not asbestos-containing material, because this lies under the vinyl layer (page 23).
- The asbestos fibres in river water are shorter than 5 μm and are therefore of no medical importance (page 28).
- A location where amphiboles were detected in the air is mentioned several times. This factory has not been processing amphiboles for years, so that this source has disappeared and it only concerns an out-of-date observation.

The conversion factor used in the comparison of the asbestos measured in the ambient air with that measured in the work situation is incorrect. The whole assessment in this report of the exposure levels in the Netherlands is based on measurements made by the TNO.
These measurements showed that only 10% of all fibres of 5 μm long are visible with the light microscope as compared with that observable with the transmission electron microscope.
The factor of 10 of Den Boeft and Lanting must therefore also be applied on page 81 and not the factor of 2 found by Cherrie in another study under different conditions.

2.2. Effects

It is stated on page 76 that mesothelioma has no known causes other than asbestos. However, other causes are mentioned in the Appendix to the report (pages 21 and 22).
Erionite (1) and radioactive radiation (2) are two established causes of mesothelioma in man.
Animal studies have even shown that, under special circumstances, many types of fibre (3) may cause mesothelioma. (The scientific literature on this subject is summarized in: Non-Asbestos Related Malignant Mesothelioma, Canadian Asbestos Information Centre.)

The start of the industrial application of asbestos dates back to the second half of the last century and not to the 1950s (page 76). It was only in the 1950s that the effects of asbestos were recognized in medical circles.

On page 110, under 9.1.1. (risks to man), the lifetime risk of mesothelioma from exposure to amphiboles is again discussed, resulting in an estimated risk thought to be over 10^{-6}. It should be noted here that the presence of amphiboles at one location was established eight years ago, and that this source has meanwhile disappeared because the factory concerned no longer processes amphiboles.

A factor of 10 should be used for the "translation" of light microscopic measurements to transmission electron microscopic measurements.

This factor is derived from the same study which produced the exposure data for the Netherlands.

An independent relationship between asbestos and lung cancer is assumed throughout the entire document.

No mention is made of the many studies which led to the conclusion that asbestos is a necessary condition for the development of lung cancer in asbestos workers.

In the last-mentioned case there is a limit, which is set at 25 fibre years (K. Browne: Is asbestos or asbestosis the cause of the increased risk of lung cancer in Asbestos workers, British J. Ind. Med. 1986, 43: 145-149).

The statement that the principal effect of asbestos on man (the Appendix even makes mention of the effect on the "general population") is cancer is entirely inconsistent with the findings of recent research. At the IARC symposium in 1987, the view gained ground that asbestosis should be regarded as a prestage of lung cancer among asbestos workers.

Neuberger, after an extensive study, concluded that the same high exposure levels are required for the development of bronchial cancer in asbestos workers as for asbestosis (Analyse von Arbeiten zur Frage der Bewertung des Gesundheitsrisikos von Asbest. Gefahrstoff-Verordnung der B.R.D. Begründung des Antrages zur Gefahrstoffe Wien, 1987).

Such concentrations not only do not occur in the ambient air but also no longer in the occupational air of the asbestos-processing industry in the Netherlands.

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APPENDIX to report no. 758473013

INTEGRATED CRITERIA DOCUMENT ASBESTOS
EFFECTS

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INTRODUCTION

Asbestos is a general term applied to certain fibrous forms ("asbestiform" varieties) of silicate minerals, with long thin separable fibers or fibrils possessing high tensile strength and flexibility. A fiber is defined as a needle-shaped particle with a length:diameter ratio (= aspect ratio) of > 3:1. Current use of the term asbestos is restricted to six fibrous silicates: chrysotile, crocidolite, amosite, anthophyllite, tremolite and actinolite.
Chrysotile belongs to the mineral group of serpentines, the other five asbestos varieties belong to the mineral group of amphiboles. Chrysotile has the molecular structure $Mg_3(Si_2O_5)(OH)_4$; the amphiboles have the overall formula $(X,Y)_7(Si_8O_{22})(OH)_2$ in which X and Y are cations, mostly Mg and Fe, but also Na, Ca, etc. Non-fibrous varieties of the mentioned six asbestos minerals have virtually the same chemical composition and basic crystal structural components, but differ in crystal form. Those varieties are usually not called asbestos; they may sometimes be called "non-fibrous asbestos" or "non-fibrous chrysotile, crocidolite etc." but they are usually indicated by their mineral names, e.g. Riebeckite (for the crocidolite mineral), Cummingtonite-Gruenerite (for the amosite mineral).
There are many other "asbestiform" minerals, with crystal-forming properties similar to asbestos, that occur naturally. They usually do not possess the same physical-chemical properties as asbestos, and hardly ever occur in sufficient quantities for exploitation. Examples of commercially applied asbestiform minerals are attapulgite and sepiolite. There are also many asbestiform man-made materials, e.g. glass wool, rock wool, ceramic fibers (Walton, 1982; NRC, 1984).
The focus of this document will be on asbestos; some attention will be paid to non-asbestos fibrous materials, but the reviewed literature on the latter subject is not exhaustive.

CAS registry number, names and synonyms of the six commercial asbestos varieties

Name	CAS nr.	Synonyms	Mineral group
Chrysotile	12001-29-5	white asbestos	serpentine
Crocidolite	12001-28-4	blue asbestos, Riebeckite	amphibole
Amosite	12172-73-5	brown asbestos, Cummingtonite-Gruenerite	amphibole
Antophyllite	17068-78-9		amphibole
Actinolite	13768-00-8		amphibole
Tremolite	14567-73-8		amphibole

1. CHEMOBIOKINETICS AND METABOLISM

1.1. Uptake

1.1.1. Oral

Animals

There has been some dispute in literature whether ingested asbestos fibres are able to pass through the gastrointestinal (GI) wall. If fibres are able to cross the GI wall, they may do so by persorption (a mechanism described by Volkheimer, 1974), or by direct penetration through the GI wall due to their sharp needle-like structure. However, experimental evidence (both qualitative and quantitative) of the penetration of ingested fibres into the bloodstream and tissues outside the GI tract is conflicting. This may partly be due to insensitive techniques, experimental artefacts and contamination (Toft et al., 1984; Cook, 1983). Data are given in tables 1 and 2. Despite these conflicting data, the observation of a time-related increase in the asbestos concentration in hepatic portal blood of rats after a single oral dose is evidence for the crossing of the GI wall that must be heavily weighted. A peak appeared 7 hours after asbestos ingestion; if the single dose was preceeded by one month of asbestos feeding the blood fibre levels were considerably higher, at all examined time intervals, but again a peak appeared at 7 hours after ingestion (Weinzweig and Richards, 1983).

The recovery of a relatively higher proportion of long fibres (> 4 μm length) from the lymph of rats, compared with the proportion of those fibres found in administered dietary chrysotile or crocidolite, suggested the preferential uptake of longer fibres from the GI tract (Sebastien et al., 1980). However, very long fibres (32-128 μm) were found in lymph that did not at all occur in feed, which is an indication of contamination or exposure from other sources that greatly reduces the importance of these findings. Contrary to these results, in studies of Weinzweig and Richards (1983) and Cunningham et al. (1977) the mean length of asbestos fibres present in rat blood was found to be smaller than the mean length of ingested chrysotile fibres. This may indicate a preferential absorption of shorter fibres, but it may also be a consequence of the breakdown of fibres in the body (see also 1.3.1.).

The highest reported fibre concentration in animal tissue was approximately 5 x 10^6 fibres/g rat blood, whereas the corresponding single intragastric dose - by coincidence the lowest asbestos dose giving positive evidence of fibre migration- was approximately 2.5 x 10^7 fibres/g body weigth (Cunningham and Pontefract, 1973). However, this dose was given by injection through the opened abdomen, which is a method very liable to damage of tissues and increase in artefactual GI absorption. From dietary studies, using much higher doses of asbestos (details presented in tables 1 and 2), the amount of fibres recovered per gram tissue was 10^{-11} -10^{-10} times lower than the corresponding cumulative ingested dose per gram body weight (calculated with a conversion factor of 10^{10} fibres per mg asbestos; Cunningham and Pontefract, 1973). The similarly calculated recovery rate of ingested fibres from rat lymph ranged from 10^{-7} to 10^{-4} (Sebastien et al., 1980). It can therefore be concluded that the proportion of ingested fibres which cross the GI wall and penetrate into tissues outside the GI tract of rats is very small.

Man

Evidence suggestive of migration of ingested fibres through the GI wall in humans is the observed relatively high fibre content of tissues and urine in residents of areas with a high asbestos concentration in drinking water. However, the results of very similar human studies are contradictory. In the study providing the most suggestive evidence of fibre penetration (Carter and Taylor, 1980), test samples -but not control samples- may have been contaminated with fibre-containing tap water (Cook, 1983). Cook and Ohlson (1979) estimated that, in a group of 8 volunteers, 1:1000 amphibole fibres ingested with drinking water were eliminated in urine, which would indicate a higher uptake than seen in animals. However, urinary recovery of the ingested asbestos-like mineral attapulgite was much lower (see 1.4.1). Data are given in table 2.

1.1.2. Dermal

The only data found concerning the uptake of asbestos or other mineral fibres through the skin were found in a review summarizing relevant Soviet literature concerning asbestos. Local invasion of asbestos fibres into the epidermis of fingers, hands, toes, soles and shins of asbestos workers was reported (IRPTC, 1982). This route of exposure may not be very important, since the skin and underlying tissues have not been reported to be involved in asbestos-related disease in humans, nor in animals, whereas cells and tissues into which fibres

are able to penetrate usually show some degree of abnormality (see 2.2 and 2.5).

1.1.3. Inhalation

Deposition

The general mechanisms by which inhaled particles may be deposited in the respiratory tract (interception, impaction, electrostatical attraction, gravitational settling, Brownian diffusion) have been described in detail in the Criteria Document "Fine Particulate Matter" (Prins et al., 1985). Although interception and electrostatical attraction are not very important for the deposition of spherical particles, they may be for mineral fibres (Lippmann et al., 1980). Deposition by interception depends mainly on fibre length; longer fibres are more easily intercepted than shorter fibres. Furthermore, freshly fractured mineral dust fibres can have an increased static electricity, which enhances deposition by electrostatic attraction in the respiratory tract (Lippmann et al., 1980). Electrostatic charging of amosite fibres caused up to 40% enhancement of dust deposition in the pulmonary region of rats (Vincent et al., 1981).

Deposition by impaction depends mainly on the aerodynamic equivalent fibre diameter (Dae), which is approximately 3-4 x larger than the actual diameter for amosite and glass fibres, and probably for all other amphiboles, and relatively independent of fibre length. For chrysotile a Dae is more difficult to assess, because chrysotile fibres tend to be curved and therefore behave differently (Gross, 1981). Particles with large Dae impact preferentially in the nasopharynx and the tracheobronchial region, although the deposition by diffusion of particles with a Dae much smaller than 0.01 μm may also be high in these regions. Particles with Dae between 0.1 and 2 μm are for a large part deposited in the alveolar region of the lungs (Lippmann et al., 1980). This relationship between mean Dae and deposition was clearly demonstrated for various asbestos types by rat single inhalation experiments (Morgan et al., 1975).

The upper limit of respirability for long fibrous particles is approximately 10 μm Dae, which corresponds with 3.5 μm fibre diameter for straight fibre types, and 200 μm fibre length. These values were established from human data (lung fibre contents) as well as from rat inhalation experiments (Lee, 1985).

The total amounts of deposited chrysotile A, chrysotile B, amosite, crocidolite, anthophyllite and a fluoramphibole in rats, expressed as

percentage of inhaled material, were 31, 43, 42, 41, 64 and 68%, respectively, of which 29-38% in the alveolar region of the lungs, 3-9% in the nasal passage, 51-67% in the GI tract (originating from clearance -see Clearance/retention), and 1-2% in the oesophagus (Morgan et al., 1975). Similar findings were reported for irradiated crocidolite in rats (Evans et al., 1973) and in Beagle dogs (Griffis et al., 1983).

Clearance/retention

The International Commission on Radiological Protection (ICRP) assumes a halftime of 4 minutes for physical clearance from the human nasopharyngeal region, which mainly takes place via the mucociliary escalator and subsequent swallowing/expectoration (Raabe, 1984).

The primary clearance mechanism in the tracheobroncheal region is also mucociliary transport and swallowing/expectoration. This can be accelerated by coughing. The approximate clearance halftime for the larger airways in this region is 0.5 hr, for intermediate airways in this region 2.5 hr and for finer airways in this region 5 hr in humans (Raabe, 1984).

Insoluble particles like asbestos, deposited beyond the ciliated airways, are removed very slowly. Halftimes of clearance of insoluble particles from the deep lung for man have been estimated from data on dogs and monkeys to be 1-2 years (Lippmann et al., 1980; Raabe, 1984). Particles entering this region are rapidly phagocytized by pulmonary macrophages; in rats, free fibres were observed entering the underlying epithelial cells, the interstitium, the basement membranes or even the endothelial cells of capillaries (Brody and Hill, 1981; Pinkerton et al., 1984). In vitro studies (see 2.5) have shown that fibres with length < 3 μm are usually completely engulfed by macrophages; fibres with length > 5 μm may be incompletely phagocytized, with part of the fibres being uncovered. Fibres with diameter > 3 μm are not taken up by macrophages (Beck and Tilkes, 1980).

Migration and grouping of particle-containing macrophages leads to redistribution of evenly dispersed particles into clumps and focal aggregations of particles, mostly in the periphery of the lung and subpleurally (Raabe, 1984). In rodents, particle-containing macrophages may be carried to the tracheobronchial region by a flow of pulmonary liquid, whereas in humans this flow appears to be only minimal (Raabe, 1984).

Gross et al. (1967) reported that intratracheal treatment with NaOH affected mucociliary clearance in rats, resulting in increased retention of inhaled fibres. The effect of smoking on the deposition and retention of asbestos is

not exactly known. Irritants in smoke may alter the properties of lung surfactant, and smoke is known to have bronchoconstrictive properties, which increase particle deposition; on the other hand, inhalation of smoke may change the breathing pattern and increase the exhalation of air and particles; enhanced mucus secretion resulting from smoking may also cause increased clearance (Lippmann et al., 1980).

Next to the minimal clearance of particles from the deep lung by transport to the ciliated airways, another possible clearance route for migrating particles and particle-laden macrophages is the pulmonary lymph drainage system (Raabe, 1984). Particles that penetrate the alveolar surface can migrate through the lymphatic drainage system to pleural, hilar and tracheal lymph nodes. This migration is very slow (several months; Lippmann et al., 1980). Wright and Kuschner (1977) reported that only short fibres (< 5 μm length) were transported to hilar lymph nodes in guinea pigs after intratracheal injection. Asbestos particles eventually trapped in the pulmonary interstitium cannot be removed or redistributed mechanically (Raabe, 1984). Ultimately all uncleared material will reside in the connective tissue, and can be seen by electron microscope as mainly subpleural foci (Lippmann et al., 1980).

Wagner et al. (1974) observed a linear increase in amphibole dust retained in rat lungs with increasing cumulative inhaled dose; this linear relationship was not observed with chrysotile (2 different types), which accumulated only to a very small extent in the lungs. Directly after termination of 6 month inhalatory exposure, the lung amphibole content was approximately the same for amosite, crocidolite and anthophyllite exposed rats (4.4-4.7 mg/animal). 18 Months later, the amounts recovered from rat lungs were 1.2 and 1.3 mg/animal for amosite and crocidolite, and 2.6 mg for anthophyllite. The differences in clearance between the amphiboles were not statistically significant.

Autopsy on groups of humans with estimated high and low occupational exposure to asbestos also suggested that more amphiboles than chrysotile are retained in the lungs, because in subjects with a long time lapse between the last exposure and autopsy, amphibole fibres were recovered in larger numbers in the lungs than chrysotile fibres. The core of asbestos bodies -see 1.3.3.- also consisted mainly of amphiboles. Chrysotile, however, was more often seen in pleural plaques (= thickened pleural foci), mainly as very short fibrils. The variation in fibre content of these pleural plaques was much smaller than the variation found in lung tissue fibre content, the latter being directly related to estimated exposure. This suggests that the migration of fibres to the pleura is relatively independent of the amount of fibres

deposited in the lungs. The proportion of fibres with length < 5 μm in lung parenchyma of these humans ranged from 70% to 90% depending on exposure: heavily asbestos-exposed subjects had a larger proportion of long fibres in lung parenchyma than those with estimated low asbestos exposure. The mean fibre length of coated (see 1.3.2. and 1.3.3.) optically visible (> 5 μm) fibres found in lung parenchyma was 51, 45 and 37 μm for subjects with high, low or no estimated exposure to asbestos, respectively; uncoated fibres were generally shorter. Chrysotile in pleural plaques was found mainly as thin "ultimate" fibrils; the mean fibre length of optically visible coated fibres in the pleura was 28 μm (Sebastien et al., 1977).

Uptake in blood

Only particles with physical diameter < 10 nm can diffuse through pores in the alveolar region into the blood (Raabe, 1984), but the possibility of larger asbestos fibres directly penetrating the alveolar tissue and the vascular endothelium cannot be excluded. Griffis et al. (1983) reported the presence of crocidolite asbestos in the blood of Beagle dogs 4 days after 60 minutes inhalation of 1.5% (v/v) neutron-irradiated crocidolite in air (cumulative inhaled dose 7-10 mg). (No further details were given; the radioactivity was probably measured in arterial blood obtained after exsanguination). From the urinary excretion data of these dogs it can be estimated that 3% of the initially deposited crocidolite -or more- must have reached the bloodstream. Since a large proportion of deposited asbestos is cleared from the lungs into the GI tract (see Clearance/retention) some fibres found in blood and urine may have passed the GI barrier. Another possibility of fibres reaching the bloodstream after inhalation is via the lymphatic system.

1.2. Distribution

1.2.1. Animal studies

The overall impression is, that there is initially no preferential distribution of asbestos fibres entering the circulation to one particular type of tissue. Intravenously injected tritiated or neutron-activated chrysotile was rapidly distributed among lungs, spleen and liver of rats within 6 minutes, and decreased in the lungs and slightly increased in the liver, spleen and muscle during the next 24 hours (Cunningham and Pontefract, 1973). Although Roe et al. (1967) found highly selective distribution of 4 subcutaneously injected asbestos varieties into the serosal membranes of the

thorax and abdomen of mice, Kanazawa et al. (1970) could not confirm this in a very similar study with mice. The latter authors have carefully examined all injection sites for inadvertent injection of asbestos into abdominal or thoracic cavities; the former did not report similar safety measures, which may be one explanation for the different results. Animal tissues in which asbestos fibres were detected at some stage after oral or intragastric administration are: liver, lungs, kidney cortex, spleen, omentum, heart, brain, pancreas and lymph nodes (Bolton et al., 1982; Patel-Mandlik and Millette, 1980; Kaczenski and Hallenbeck, 1984; Cunningham and Pontefract, 1973). Shortly after single inhalation of neutron-irradiated crocidolite the liver and head (no details given) of Beagle dogs showed radioactivity (Griffis et al., 1983).

In the long term, fibres retained in tissues may be redistributed into lymph nodes and subserosal foci, as was already described for inhaled fibres in lung tissue. Kanazawa et al. (1970) showed that the migration of asbestos fibres away from the site of subcutaneous injection takes place mainly along lymphatic pathways, and some fibres could be detected in subpleural foci in longterm survivors of their study.

In all cases the reported tissue fibre concentrations were low. Fibres recovered from tissues were not consistently different in size from the administered fibres.

1.2.2. Human studies

Cunningham and Pontefract (1973) examined the tissues of 3 humans from the general population, with no history of occupational exposure to asbestos, who had died from natural causes (no other details given). They found levels of 1.1-3.8 x 10^5 chrysotile fibres /g brain, 0-2.5 x 10^5 fibres/g spleen and 7.7-9.2 x 10^5 fibres/g peritoneum. Autopsy data reported by Carter and Taylor (1980) for a group of residents from an area with high amphibole content in drinking water may not be reliable because of sample contamination (Meek, 1983).

1.2.3. Placental transport

Asbestos fibres were demonstrated to be able to cross the placenta of rats: after a chrysotile suspension in water had been injected into the femoral vein of pregnant rats at 2 day intervals beginning on the 10th to 14th day of gestation, the fibre content of foetal livers and lungs was significantly

higher in the experimental group than in the control group (Cunningham and Pontefract, 1974).

1.3. Biotransformation

1.3.1. Degradation

Ingested chrysotile fibres may be altered by contact with gastric juice and probably also with other body fluids. It was observed that magnesium (and nickel) ions leach out as a result of exposure to water for prolonged periods, to strong acids and to simulated gastric juices, leaving a magnesium-free silica network. The gross crystallinity of the fibres is thus destructed and they become more fragile. The smaller the fibre diameter, the faster this loss is (Seshan, 1983; Saxena et al., 1982). Similar degradation of fibres may also occur in lung tissue. Jaurand et al. (1984) demonstrated that leaching of Mg from chrysotile fibres occurred within rabbit alveolar macrophages and rat pleural mesothelial cells in culture. The kinetics of Mg-leaching in the macrophages resembled those in a medium of pH 4, whereas the kinetics in pleural cells resembled those in a medium of pH 7.
Furthermore, fibres of chrysotile tend to fragment longitudinally into thinner fibrils in the body (NRC, 1984). Amphibole fibres are much more resistent to both forms of degradation.

1.3.2. Coating

The surface characteristics of fibres in the body may be modified by adsorption of compounds like mucin (in the GI and higher respiratory tract) and lung surfactant (in the lower parts of the lungs), which adsorb onto the fibres and have effect on the surface charge and the leaching of magnesium, and hence reduce possible cytotoxic properties of the fibres. Complex organic compounds such as muco- and glycoproteins may do the same in the GI tract (Seshan, 1983; NRC, 1984).

1.3.3 Asbestos body formation

The formation of "asbestos bodies", which is sometimes also called coating, is an intracellular process. A fibre becomes incorporated into the intracytoplasmic vacuole (phagosome) of a macrophage or giant cell (= two or more fused macrophages) and a mucopolysaccharide matrix is deposited on the fibre. Iron accumulates in the coating initially as hemosiderin. Finally the cell dies and the yellow iron-protein coated body is released into the

pulmonary parenchyma, where it remains as biologically insignificant, probably inert matter. Occasionally, asbestos bodies are also seen in other parts of the body. Fibres with a length of less than 5-10 μm are rarely coated; since chrysotile tends to fragment more than amphiboles this is probably why the core of asbestos bodies found in the general population usually consists of amphiboles (Churg and Warnock, 1981; Rebuck and Braude, 1983). Because the core may also contain other minerals than asbestos, a more general name is "ferruginous bodies". Ferruginous bodies can be found from 3 weeks after exposure onwards (Holt, 1982).

The presence of asbestos bodies in broncheo-alveolar lavage fluid (BALF) is often used to estimate the past exposure of humans to asbestos. However, this is only a very rough estimate, which cannot be used for assessment of dose-response relations: only long fibres are coated to form bodies whereas a considerable proportion of fibres may consist of very short fibres; the ratio bodies/total fibres found in human lungs is quite variable (Sebastien et al., 1977; Churg and Warnock, 1981).

1.4. Excretion

1.4.1. Oral

Animals

The major part of asbestos recovered from the feces of rats fed 100 mg/kg chrysotile, crocidolite or amosite for 1 month was excreted within 48 hours after termination of the experiment. No more asbestos could be detected in fecal pellets after 7 days (Bolton and Davis, 1976). After 28 days, asbestos could not be detected in the intestines and intestinal contents. The urinary excretion of asbestos was not measured; however, since GI absorption was shown to be very low in rats, fecal excretion of asbestos probably covered the major part of the intake. Data on the urinary excretion of asbestos in animals after ingestion are not available.

Man

The fecal excretion of asbestos or other mineral fibres after ingestion was not studied in humans, but it can safely be assumed that the major part of ingested asbestos will be excreted in feces, like in animals, since GI absorption was very low. For people drinking water with a high amphibole content, urinary amphibole excretion was significantly higher than for people

drinking filtered or uncontaminated water but it was still very low (0.1% of total ingested amphibole). For 2 persons switching from a high to a low amphibole intake via drinking water, the urinary amphibole excretion decreased correspondingly (Cook and Ohlson, 1979). A comparable excretion pattern could not be found for chrysotile (Boatman et al., 1983; Cook and Ohlson, 1979); this may be due to contamination of control samples with chrysotile, or to equal exposure of the experimental and control groups by e.g. air and food (in which chrysotile is more common than ampbiboles). The urinary concentration of attapulgite of a woman that had received the mineral as a drug for 6 months (9000 mg/day) was 3 x 10^5 fibres/ml (Bignon et al., 1980). Using a conversion factor of 10^{10} fibres per mg asbestos (Cunningham and Pontefract, 1973) and assuming a urinary production of 1.5 l/day, it can be calculated that this is about equal to a daily urinary attapulgite excretion of 0.045 mg/day which is only 0.0005% of the daily intake.

1.4.2. Inhalation

Animals

Rats exposed to irradiated crocidolite showed a rapid and a slow phase of fecal excretion of radioactivity. The rapid phase had a halftime of 0.43 day; this obviously represented clearance of the upper part of the respiratory tract. The slow phase, possibly representing clearance of the alveolar region of the lungs via the GI tract, had a halftime of 29 days. When animals were killed 30 days after exposure, 75% of radioactivity present in the organism immediately after exposure had been excreted in the feces (Evans et al., 1973). Rats exposed to neutron-irradiated anthophyllite showed a fecal excretion of radioactive anthophyllite after 14 days amounting to 1.4%/day of the lung content. After 120 days this had fallen to 0.5% daily (Morgan et al., 1978). Beagle dogs exposed to neutron-irradiated crocidolite excreted approximately 70% of the initial body burden within 4 days after exposure. 96% Of this activity was in the feces, and therefore 4% probably in urine (Griffis et al., 1983).

Man

Humans, exposed occupationally to high, moderate and low chrysotile air concentrations, had an average fibre content in feces of 26.47 x 10^6, 11.93 x 10^6 and 0.37 x 10^6 fibres/g feces, respectively. The fibre content of the feces was thus significantly higher in higher exposure groups (Cunningham et

al., 1976). Human data on urinary excretion of fibres after inhalation were not available, although they may be important for a better quantification of the amount of inhaled fibres that reach the bloodstream and other tissues.

1.5. Summary and conclusions

Ingestion

There has been some dispute whether asbestos fibres are able to cross the gastrointestinal wall after ingestion. Rat experiments have indicated that the major part of ingested asbestos is excreted into the feces within 48 hours after ingestion (Bolton and Davis, 1976). However, a minor part of ingested, intact asbestos fibres may penetrate into the gastrointestinal wall, or cross the gastrointestinal wall and reach the bloodstream and various tissues and organs. The results of experiments with rats and baboons, investigating this passage of fibres through the gastrointestinal wall after ingestion, are difficult to evaluate. There are many possibilities of confounding contamination of tissues with asbestos, and the available analytical techniques are not very sensitive. Nevertheless, the observed time-related increase in the asbestos concentration of hepatic portal blood of rats until 7 hours after asbestos ingestion indicates that passage of fibres from the gastrointestinal tract into blood does occur (Weinzweig and Richards, 1983).
Animal tissues outside the gastrointestinal tract in which asbestos fibres have been detected after oral or intragastric administration are the liver, lungs, kidney cortex, spleen, omentum, heart, brain, pancreas and lymph nodes (Bolton et al., 1982; Patel-Mandlik and Millette, 1980; Kaczenski and Hallenbeck, 1984; Cunningham and Pontefract, 1973). There is no preference for one particular type of tissue, although there are some indications that fibres residing in the tissues are gradually redistributed towards subserosal foci and lymph nodes.
Chrysotile fibres reaching the stomach after ingestion may be partly broken down by the dissolving action of gastric juice. In the tissues, chrysotile asbestos may be similarly dissolved, or fragmented into small fibrils. In contrast, amphibole asbestos fibres are much more resistent to degradation in the body.
The quantitative recovery of ingested fibres from the various tissues was generally very low. In three independent rat studies, the maximum amount of fibres recovered per gram tissue was 10^{-11}-10^{-10}x smaller than the cumulative ingested amount of fibres per gram body weight (Bolton et al., 1982;

Cunningham et al., 1977; Gross et al., 1974). The maximum recovery rate of ingested asbestos fibres from rat lymph was also very low (Sebastien et al., 1980). The mean fibre length of fibres recovered from tissues was not consistently different from that of ingested fibres.

In humans, the uptake of ingested fibres from the gastrointestinal tract was demonstrated by recovery of fibres from urine. The urinary amphibole fibre concentration directly reflected the intake from drinking water in volunteers switching from a high to a low amphibole intake. The maximum reported urinary excretion, however, was very low (0.1% of total ingested fibres; Cook and Ohlson, 1979). Cunningham and Pontefract (1973) analysed the spleen, brain and peritoneum of three humans from the general population with no history of occupational exposure to asbestos. Although chrysotile fibres were found (in concentrations ranging from 0 to 9.2×10^5 fibres.gram^{-1} tissue), these cannot be related to exposure.

In conclusion, it can be stated that only a very small proportion of ingested asbestos fibres will pass the gastrointestinal wall and will be excreted into urine; only few fibres penetrate into tissues and are retained there. The major part of ingested asbestos will be excreted into the feces.

Inhalation

Two mechanisms of deposition in the respiratory tract are important for inhaled asbestos fibres: interception, which mainly depends on fibre length, and impaction, which is dependent on the mean aerodynamic equivalent fibre diameter (Dae) but relatively independent of fibre length. The Dae is approximately 3-4 x larger than the actual diameter for straight fibres (Gross, 1981). The upper limit of respirability for fibres is a Dae of 10 μm, which corresponds with an actual fibre diameter of approximately 3 μm for amphiboles, and a fibre length of 200 μm (Lee, 1985).

Particles with a large Dae and/or large fibre length, and particles with a very small Dae (< 0.1 μm), are deposited preferentially in the nasopharynx; particles with a Dae of > 2 μm are mainly deposited in the tracheobronchial region. These parts of the respiratory tract are mainly cleared via the mucociliary escalator into the gastrointestinal tract, which occurs relatively rapid (hours). Particles with a Dae between 0.1 and 2 μm are deposited almost exclusively in the alveolar region of the lungs, beyond the ciliated airways. Clearance from this region is much slower, and may take months to years (Raabe, 1984; Lippmann et al., 1980).

Most fibres with a length < 3 μm entering the alveolar region of the lungs are rapidly phagocytized by pulmonary macrophages, but free fibres may also enter cells of the epithelium, interstitium, or endothelium of capillaries. In vitro studies indicate that fibres longer than 3-5 μm may be phagocytized incompletely, with part of the fibres remaining uncovered (Beck and Tilkes, 1980). Only a small proportion of particle-containing macrophages will be transported to the ciliated airways; most macrophages, as well as free fibres, are slowly migrating towards the periphery of the lungs and to the pleura, where the asbestos fibres finally remain. Some fibres, mainly the longer ones (> 5-10 μm length), are coated and form inert asbestos bodies, but many uncoated fibres can be found in lung tissue. Both rat studies and observations in humans suggest that amphibole fibres accumulate to a larger extent in the lungs than chrysotile fibres (Wagner et al., 1974; Sebastien et al., 1977). Chrysotile fibres are probably partially dissolved, whereas amphibole fibres are not. Chrysotile may also split into thinner fibrils in lung tissue, which are not easily detected.

Studies with rats and dogs have demonstrated that a large part (70-75%) of asbestos deposited in the lungs after inhalation will be excreted in the feces. The fecal excretion of inhaled asbestos shows a rapid phase, corresponding with the rapid mucociliary clearance from the lungs into the gastrointestinal tract, and a very slow phase, which probably represents a very gradual clearance from the alveolar region of the lungs (Evans et al., 1973; Morgan et al., 1978; Griffis et al., 1983). The fecal excretion of asbestos by humans also reflects inhalatory exposure (Cunningham et al., 1976). Unfortunately, data on urinary excretion of asbestos after inhalatory exposure are not available.

Summarizing, it can be concluded that respirable asbestos particles with a Dae of 0.1-2 μm, and relatively independent of fibre length, have a high possibility of reaching the alveolar region of the lungs, where clearance is very slow. Many uncleared particles will migrate to the periphery of the lung and the pleura. Whereas chrysotile may be partly dissolved, or fragmented into smaller fibrils, amphibole fibres are probably not greatly altered during residence in lung tissue, and remain there permanently.

2. EFFECTS ON ANIMALS

2.1. Acute/shortterm toxicity

The effects of single or shortterm asbestos exposure are only of relevance in the context of longterm (fibrogenic or carcinogenic) effects and will therefore not be described under the heading of acute or shortterm toxicity.

2.2. Longterm toxicity/carcinogenicity

2.2.1. Oral studies

Noncarcinogenic effects

Jacobs et al. (1978) observed cellular damage of the mucosal lining of the rectum, colon and ileum (villi) after feeding chrysotile to rats for either 1 week or 14 months, as was indicated by increased DNA levels in the intestinal lumen. Others did not find any microscopic lesions of the GI tract of rats in either shortterm (Meek and Grasso, 1983) or longterm (e.g. Bolton et al., 1982) studies.

Some investigators studied cellular proliferation in the GI tract in rats and monkeys after single or repeated oral doses of asbestos (in comparison with the fibrotic reaction of lung tissue after inhalation) by measuring the incorporation of tritiated thymidine. Some changes of thymidine incorporation into the wall of various parts of the GI tract and in pancreas and liver were observed after various time intervals, but there was no consistent picture and definite conclusions can therefore not be drawn (Amacher et al., 1974, 1975; Epstein and Varnes, 1978; Jacobs et al., 1977; Bolton et al., 1982).

Carcinogenic effects

In a critical review Toft et al. (1984) used a scoring system to weight the results of well- and less well-designed oral carcinogenicity studies, and found no conclusive evidence that asbestos is carcinogenic to animals after ingestion. Since their evalution, some new relevant data have been published. In table 3 the available quantitative oral carcinogenicity studies with asbestos are summarized. Some available material was not included in the table for various reasons. Two studies were considered inadequate: Cunningham et al. (1977) found positive results in a study with only 10 animals, which could not be reproduced in a later study with larger groups; Gibel et al. (1976) used asbestos filter material which was not pure and could have been contaminated

with (other) carcinogens responsible for the positive effects. A "qualitative" study, in which rats reveived tap water of various origins and lake sediments with different, not very well-quantitated amounts of naturally occurring amphibole fibres, failed to show any carcinogenic effects (Hilding et al., 1981). Some studies included treatment with a known intestinal carcinogen (e.g. 1,2-dimethylhydrazine - DMH) to investigate the possible tumor-promoting or cocarcinogenic properties of asbestos, but the results cannot be properly evaluated because of the very high background tumor incidence caused by these initiating carcinogens; nevertheless, they do not suggest that asbestos is a promoter or cocarcinogen after oral exposure (NTP, 1985; McConnell et al., 1983b; Ward et al., 1980).

Some studies that were not quite up to accepted standards -with respect to the type or amount of animals used or the duration of the administration period- were included in table 3 because they are frequently referred to in literature; omission of these studies would make the remaining number of studies very small, but it would not alter the final conclusion. In the studies summarized in the table, only few statistically significant effects have been found. They will be briefly discussed below.

In hamsters receiving 1% dietary chrysotile of two different fibre sizes (shortrange and intermediate range) for lifetime, an increased incidence of primary tumors was observed in both groups which could be ascribed mainly to the increased incidence of adrenal cortical adenomas. This increase was significant only when compared with pooled controls, not with concurrent controls (McConnell et al., 1983a). However, in this study DMH, a wellknown intestinal carcinogen in rats (NTP, 1985) and also in a pilot study with hamsters (McConnell et al., 1983a), did not produce any increase in intestinal tumors either. This raises serious doubts about the suitability of the animals used in this study for the detection of GI cancers. It also has to be noted that hamsters are relatively insensitive to the effects of asbestos via other routes of exposure (NRC, 1984). In another study with hamsters (the only available study designed to find a possible dose-response relationship) 2 early squamous-cell carcinomas of the forestomach and 1 peritoneal mesothelioma were found in the mid dose group, whereas no similar tumors were seen in the high or low dose group (Smith et al., 1980, cited by IPCS, 1986). The evidence of hamster oral carcinogenicity studies can therefore be considered as negative, but hamsters may not be the most sensitive species.

In F344 rats, the incidences of C-cell carcinomas of the thyroid and of mononuclear leukemia were increased after lifetime feeding of 1% amosite, in

males only; males fed amosite for lifetime with preweaning gavage of chrysotile also had increased mononuclear leukemia, but no increased C-cell carcinomas of the thyroid (McConnell et al., 1983b). However, it must be noted that both types of tumors frequently occur in this particular strain of rat, and that the effects were not significant in females. Since the incidence of GI tumors in these studies was not different for treated and control animals, it was concluded that the observed tumors were not treatment-related.

A slight support of tumorigenic effects of ingested asbestos may be the incidental occurrence of mesotheliomas (which is normally very rare but has been demonstrated after intrapleural/intraperitoneal injection of asbestos): 1/189 mesothelioma in the abdomen was reported in F344 rats on a lifetime diet containing 10% chrysotile B (Donham et al., 1980), 1/60 peritoneal mesothelioma was described in hamsters receiving 5 mg amosite/l drinking water for lifetime (Smith et al., 1980, cited by IPCS, 1986), 1/30 pleural mesothelioma occurred in a group of rats fed asbestos (50 mg/kg b.w.) and 1/30 peritoneal mesothelioma was reported in rats fed diatomaceous earth (50 mg/kg b.w.) -which is a constituent of water filters commonly used for drinking water filtration with unknown particle structure- for lifetime (Hilding et al., 1981); mesotheliomas were not observed in any of the untreated control animals. Another type of tumor reported in 2 different studies, in asbestos- or talc[1]-treated animals, was leiomyosarcoma of the stomach (1/24 rats fed 90 mg/kg amosite for lifetime - Bolton et al., 1982; 1/32 rats fed 250 mg/kg talc for 101 days, and 1/32 rats fed 250 mg/kg superfine chrysotile for 101 days - Wagner et al., 1977). However, since these effects were far from significant, even in longterm studies with high dose levels and relatively large amounts of test animals, they cannot by themselves be considered as evidence for carcinogenicity by the oral route.

Significantly increased incidences of benign neoplasms which may be directly related to the ingestion of asbestos were reported in 2 studies in male rats fed chrysotile for lifetime. At approximately 90 mg/kg/day chrysotile A benign neoplasms were observed mainly as hemangiomas of the mesenterium (Bolton et al., 1982); at a dose of approximately 500 mg/kg/day intermediate range chrysotile benign adenomatous polyps were seen in the epithelium of the descending colon, but the incidence was significanty different only from

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1) Talc may contain traces of tremolite or actinolite asbestos.

pooled controls, not from concurrent controls (NTP, 1985). It must be noted that the overall tumor incidence was extremely high in this study (almost 100% of control as well as treated animals had primary tumors); this was not commented on in a peer review accompanying the final NTP report. Based on the latter study, the US EPA has recently concluded that there is limited evidence (namely, the occurrence of benign adenomatous polyps in the colon of rats) for carcinogenicity of asbestos of intermediate[1] but not of short[2] fibre length, whereas in drinking water only relatively short[3] fibres have been found (EPA, 1986). A significantly increased incidence of malignant neoplasms of the colon, however, was not reported in any study, not even by Donham et al. (1980), who concentrated in their study on possible malignant effects on the colon, and used an extremely high dose (10% in feed for lifetime). The biological relevance of these benign neoplasms is therefore doubtful, especially since they were only observed in males, in numbers significantly different only from pooled controls, not from concurrent controls.
In conclusion, it can be stated that the available studies do not indicate that asbestos is carcinogenic in rats and hamsters after ingestion.

2.2.2. Inhalation/intratracheal studies

Carcinogenicity, qualitative

There is sufficient evidence from experiments with rats, mice, hamsters, guinea pigs and rabbits that all asbestos types are carcinogenic in animals after inhalation (IARC, 1977), although there appear to be species differences: in rats and mice both benign and malignant tumors of the lungs are found, whereas hamsters, guinea pigs and rabbits seem to develop only benign neoplasms in the lungs (NRC, 1984). The types of tumors most often associated with asbestos exposure in rats and mice are adenomas, adenocarcinomas and squamous-cell carcinomas of the lung. (For the following quantitative evaluation of carcinogenicity, only the malignant tumors were considered). In addition to the above mentioned tumor types, mesotheliomas of the pleura are frequently noted; mesotheliomas of the peritoneum are also seen

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1) ± 60% fibres > 5 μm length; maximum length 780 μm

2) ± 20% fibres > 5 μm length; maximum length 51 μm

3) average length 0.8-4.3 μm; maximum length 80 μm

occasionally. The increase in mesotheliomas is often not statistically significant, but it is a very rare type of tumor that is almost exclusively associated with asbestos, both in humans and in animals (see 2.2.3 and 3.). Animal experiments do not confirm the observations from epidemiological studies that the GI tract is involved in asbestos-related carcinogenesis after inhalation.

Carcinogenicity, quantitative

- Mass concentration-response relationship.
  Davis et al. (1978) demonstrated that the frequency of lung tumors in rats from asbestos inhalation was concentration- related: 2 mg/m^3 chrysotile for 1 year caused 5% lung tumors (1/42 adenocarcinoma, 1/42 squamous carcinoma), whereas 10 mg/m^3 caused 20% lung tumors (6/40 adenocarcinomas, 2/40 squamous carcinomas). None of the other animal inhalation studies were designed to find a concentration-response relationship: only one asbestos concentration was studied at a time. If the different studies are compared with each other, a clear relationship between the mass concentration of asbestos in air and tumor incidence seems to be absent (see table 4). This may partly be due to a different fibre count per weigth unit of the asbestos varieties used in different studies. This will be discussed in the following paragraph.
- Fibre concentration-response relationship.
  The asbestos used in animal experiments is sometimes milled, which causes a reduction of the number of fibres detectable by light microscope (> 5 μm length) and an increase in submicroscopic fibres and in nonfibrous dust. Besides, Davis et al. (1978) observed that concentrations of more than 10 mg/m^3 asbestos in air may produce unrespirable flocs. These observations illustrate that similar mass concentrations asbestos may give very different fibre concentrations (see table 5). In table 5 the carcinogenic effects of asbestos are related to fibre concentration (rather than mass concentration) in air.
  At levels of 5.5 and 4.3 x 10^6 f/l, very similar to the level of 3.9 x 10^6 f/l for chrysotile, amosite and crocidolite produced 0/43 and 1/43 lung tumors and no mesotheliomas, whereas chrysotile produced 2/42 lung tumors and 1/42 mesothelioma in rats after 1 year inhalation (Davis et al., 1978). In the study of Reeves et al. (1974), the frequency of tumors of the lungs and pleura produced by chrysotile (7%) was very similar to that caused by crocidolite and amosite (7-9%), but at a 15-20 x lower fibre level. These

results show that differences in fibre concentration alone between comparable inhalation studies with asbestos can apparently not account for the observed differences in carcinogenicity; as intrapleural/intraperitoneal studies have indicated, fibre size may also play a role (see 2.2.3.). This will be discussed in the following paragraph.

- Fibre size.

  Both studies discussed above suggest that chrysotile is a more potent inhalatory carcinogen than the amphiboles. However, chrysotile in the study of Davis et al. (1978) had a much higher proportion of longer fibres than crocidolite and amosite (> 5 μm: 35% versus 15-18%; > 20 μm: 5% versus 0.3-0.5%). (Reeves et al. did not report the fibre sizes of the asbestos used). Recent experiment of Davis et al. (IARC, 1987; IPCS, 1986) showed that one particular type of asbestos with different fibre size may give a completely different response after inhalation: of two amosite varieties with different fibre size distribution (30% and 1% fibres > 5 μm length), tested by inhalation in rats, the variety with the longer fibres produced significantly more lung tumors than the shorter variety (> 30% and 0 lung tumors, respectively). Very similar observations were made with chrysotile. These data confirm the results from many intrapleural and intraperitoneal studies with asbestos and other fibrous materials that long fibres have a larger carcinogenic potency than short fibres (see 2.2.3.). The length of inhaled fibres is obviously very important in carcinogenicity. In inhalation studies, less attention was paid to fibre diameter than to length, but intraperitoneal and intrapleural studies indicate that fibre diameter is also important (see 2.2.3.). A comparison between different asbestos types with respect to their carcinogenic potency cannot be made without a proper fibre characterization.

- Time-response relationship.

  Wagner et al. (1974) found an approximately linear relationship between the duration of exposure to one particular type -and concentration- of asbestos and the incidence of lung tumors in rats. Data are summarized in table 6. For mesotheliomas, this relationship with the duration of asbestos exposure is probably not linear: two mesotheliomas could be found in groups of 49 rats exposed for only 1 day to crocidolite and amosite, respectively, after 1 year. This is in accordance with the observations from human occupational studies, in which mesotheliomas appear to be exponentially related to the time from first exposure (see 3.2.1.).

- Intermittent versus more continuous exposure.

Davis et al. (1980) investigated possible differences in the responses of rats exposed for 1 year to either intermittent high "peak" concentrations or more continuous "even" concentrations of chrysotile and amosite, with all groups ultimately receiving the same cumulative fibre dose. They found no significant differences in tumor incidence between the groups. However, the incidence of lung tumors observed in all groups was probably not high enough to find statistical significance. Details are given in table 7.

Carcinogenicity, synergistic effects

A strong synergistic effect of asbestos and cigarette smoke, which has been reported in epidemiologic studies with asbestos workers (see 3.2.1), could be reproduced in intratracheal studies with rats: combined intratracheal treatment of rats with asbestos and cigarette smoke or chemical carcinogens such as polycyclic aromatic hydrocarbons caused a more than additional increase in lung tumors compared to treatment with those chemicals alone (NRC, 1984; Shabad et al., 1974). Similar findings were reported for dogs (IPCS, 1986).

It has been suggested that carcinogens bind to the surface of asbestos fibres and thus have an easier access to cells: chrysotile, for example, has been demonstrated to bind a range of environmental carcinogens more strongly than other asbestos and nonasbestos fibres (Harvey et al., 1984). It is also possible that inhalation of chemicals and cigarette smoke alters the deposition, clearance and/or retention of fibres in the respiratory tract (see 1.1.3.).

Carcinogenicity, non-asbestos fibers

Recent results of a rat inhalation study with erionite from Oregon have shown that this non-asbestos fibrous mineral is extremely potent in causing pleural mesotheliomas (in 27 out of 28 animals still alive after after 12 months inhalation), whereas crocidolite of very similar fibre length distribution (53-56% of fibres > 5 μm length; 0.5-0.8% > 20 μm) and a larger fibre concentration in air (1.6×10^6 f/l versus 3.5×10^5 f/l) did not produce any mesotheliomas and only 1/28 adenocarcinoma. The proportion of very thin fibres (diameter < 0.2 μm), especially of those fibres < 10 μm length, was significantly higher for erionite (42% versus 22% for crocidolite), which may be a possible explanation for the very high potency to induce mesotheliomas. In a group rats treated with synthetic "nonfibrous" erionite, 1/28 pleural mesothelioma and 1/28 adenocarcinoma were found, which suggests that other

mechanisms not related to the fibrous structure may also play a role (Wagner et al., 1985). However, it cannot be completely excluded that the nonfibrous mineral contained a small number of biologically active fibres.
Preliminary results (reported directly after termination of exposure) with the asbestiform minerals attapulgite, with approximately 1% fibres > 5 μm length, and sepiolite, with 100% fibres < 5 μm length, suggest that these minerals are not carcinogenic in rats after inhalation for 1 year; however, definite results have not yet been published. The variety of attapulgite -but not of sepiolite- that was used did produce mesotheliomas in rats after intrapleural injection (see 2.2.3.; Wagner, 1982).
Several types of man-made mineral fibres (MMMF) like glass wool, rock wool and glass microfibres were also tested in animal inhalation studies; although some varieties had fibre sizes similar to the concurrently tested asbestos types, and some were able to produce small amounts of lung tumors, MMMF generally produced less tumors than the positive control samples of asbestos. (NRC, 1984; Wagner, 1982). It was suggested that this may be a matter of solubility. Asbestos fibres have a very low solubility, whereas fibrous glass, for example, may be more or less solubilized after prolonged stay in the lungs, depending on the variety. However, the fibre concentrations of asbestos and MMMF in the indicated studies were not always comparable and a quantitative comparison is therefore not allowed.

Fibrogenicity, qualitative

The earliest lesion reported in relation to asbestos inhalation was the occurrence of a characteristic type of fibrosis of the lungs, also called asbestosis. The most important inhalation and intratracheal studies concerning asbestosis are summarized in the tables 8 and 9; some features will be briefly discussed below.
Asbestosis has been reported to occur in all animal species after inhalatory or intratracheal exposure to asbestos (rats, mice, guinea pigs, hamsters, rabbits, gerbils, monkeys, sheep) although the degree of asbestosis may vary for different species (Reeves et al., 1974; Wagner, 1963; Wehner et al., 1979; Begin et al., 1982, 1983).
The initial event in asbestosis is the mobilization of pulmonary macrophages and polymorphonuclear leukocytes in areas of the lungs where asbestos fibres accumulate, which may partly be caused by the release of chemotactic factors by macrophages that have phagocytosed asbestos fibres and are destructed by a cytotoxic action of the fibres (Le Maho et al., 1984). The macrophages and

leukocytes aggregate initially in and around the terminal bronchioles, giving an inflammation-like reaction; the deposits become enmeshed in a fibrin network that is gradually replaced by collagen (Davis et al., 1978; Wagner et al., 1974). There is a shift from the presence of mainly type I cells towards a larger proportion of granular pneumocytes (type II cells) in the alveolar epithelium. The bronchiolar and alveolar walls thus become thickened. This type of lesion, which may be considered to be the first stage of asbestosis, was called "peribronchiolar fibrosis" by Davis et al. (1978).

At a later stage (months after first exposure to asbestos), fibrotic reactions expand to other parts of the lungs, and the diffuse focal fibrosis of the lung interstitium ("interstitial fibrosis") and of the pleura, which are characteristic of asbestosis, become manifest. In time, partial or sometimes complete obstruction of the small airways with consequent decreased lung capacity results (Begin et al., 1982, 1983; Glassroth et al., 1984). Some authors reported the occurrence of small foci of calcium phosphate accumulation ("microcalcifications") in the interstitium of rats after chrysotile -but not crocidolite- inhalation (Brody and Hill, 1982; Ogisho et al., 1984). Calcification is a well-known response to toxic interactions with cell membranes; it has been suggested that the positively charged Mg-ion of chrysotile fibres causes such an interaction (Brody and Hill, 1982), and also that membrane damage is caused by adsorption of cell membranes onto the fibres rather than by Mg-interaction (Jaurand et al., 1983; see also 2.5.). The formation of pleural calcified plaques, which is frequently described for asbestos workers, has not been reported to occur in laboratory animals (NRC, 1984).

As described in the chapter Chemobiokinetics and Metabolism (1.1.3.), most fibres retained in the lungs will move from the terminal bronchioli towards the the periphery of the lungs, into the interstitium and pleura, and remain there. This is possibly the reason why interstitial fibrosis develops only slowly and can still be seen progressing in rats 1-1.5 years after termination of exposure, whereas peribronchiolar fibrosis does not develop any further or is even regressing with time (Wagner et al., 1974; Davis et al., 1978). Several authors reported a reduced lifespan in animals with asbestosis; animals dying before termination of an experiment usually had more severe asbestosis than animals sacrificed at similar time intervals. It can therefore be concluded that asbestosis is an irreversibly progressing disease.

Fibrogenicity, quantitative

- Dose-response relationship/fibre size.

  Chrysotile, crocidolite and a synthetic amphibole with only a small proportion of fibres > 5 μm length did not produce any asbestosis in rats and guinea pigs, whereas the same asbestos type with a large proportion of fibres > 5 μm length caused significant fibrotic reactions after 1-8 intratracheal instillations (see table 9). Inhalation studies with various asbestos types in rats and mice gave similar results, with more and longer fibres producing more severe asbestosis (Davis et al., 1978; Reeves et al., 1974; Davis, cited by IPCS, 1986). Like in carcinogenicity, the degree of asbestosis therefore seems to be directly related to fibre size and fibre concentration.

- Time- response relationship.

  The degree of asbestosis in rats was demonstrated to have a positive correlation with the duration of inhalatory exposure to asbestos (Wagner et al., 1974). However, the disease also progresses after termination of exposure. Both effects are illustrated in fig. 1 (Wagner et al., 1974). Brody and Hill (1981, 1982) observed a distinct pulmonary reaction in rats after only 1 hour inhalation of 15 mg/m^3 chrysotile (3% fibres > 20 μm length), at various time points up to 1 month after inhalation. The observations included macrophage induction and aggregation, thickened alveolar duct walls and interstitial calcifications. The earliest reported observation in animal experiments of fibrin formation was already 2 hours after single intratracheal injection of amosite in guinea pigs (Dodson et al., 1983). Many other intratracheal studies also showed serious fibrotic lesions at some time point after one single intillation. These observations implicate that the time since first exposure to asbestos may be just as important for the observed degree of lung fibrosis as the duration of exposure.

- Intermittent versus continuous exposure.

  1 Year inhalatory exposure of rats to high peak concentrations of chrysotile and amosite (10 and 50 mg/m^3, respectively, for 1 day/week) resulted in an approximately 2x higher degree of interstitial fibrosis 17 months after termination of exposure than even exposure to lower doses (2 and 10 mg/m^3, respectively, for 5 days/week; peribronchiolar fibrosis was also different for the different exposure regimens, but not consistently). Thus, inhalation of high asbestos concentrations at separate occasions may produce more severe asbestosis than more continuous inhalation of lower concentrations if

the cumulative inhaled concentrations are similar (Davis et al., 1980). This is in line with the observations made earlier concerning time-response relationships.

Fibrogenicity, no-effect level

The lowest asbestos concentration studied in animals (1 mg/m^3 chrysotile, with 99% fibres shorter than 5 μm ; concentration of fibres longer than 5 μm: 3000 f/l), inhaled for 18 months did not cause any fibrotic reactions in rats (Platek et al., 1985). However, the same mass concentration with a slightly higher concentration of fibres longer than 5 μm (1.3×10^4 f/l) did cause minimal fibrosis in hamsters after 15 months inhalation (Wehner, cited by IPCS 1986). In the latter study, no indication was given of fibre size.

Fibrogenicity, non-asbestos fibers

Inhalatory exposure of rats to the asbestiform mineral attapulgite caused lung fibrosis to the same degree as crocidolite (Wagner, 1982; preliminary results, no other details given). The degree of fibrosis did not seem to be significantly different at 3, 6 and 12 months exposure for any of the fibres tested; it is not known whether fibrosis proceeded after termination of exposure.

Italian talc[1] caused fibrosis in rats to a similar degree as SFA chrysotile after inhalation for 1 year (Wagner et al., 1977); however, the amount and size distribution of fibres were not given.

In a study comparing the pulmonary response of rats to chrysotile and various man-made mineral fibres (MMMF), all tested MMMF gave some degree of fibrosis although the response was higher for chrysotile at all time intervals. However, the reaction with chrysotile was more severe after 12 months exposure than after 3 months, whereas the MMMF gave very little change with time (Wagner, 1982).

In another study, comparing amosite and various types of MMMF, the pulmonary response including fibrosis was generally much higher in the amosite group. Nevertheless, the response to MMMF appeared to be dose-related (Lee et al., 1981).

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1) Talc may contain tremolite or actinolite asbestos.

Summarizing, it can be concluded that the results obtained so far with non-asbestos fibres indicate that many non-asbestos fibres are able to induce a dose-related fibrogenic response after inhalation or intratracheal instillation, to a similar or lesser degree than the various asbestos types, depending on the material. There are some indications that fibrosis induced by MMMF is not progressive.

2.2.3. Intraperitoneal/intrapleural studies

Carcinogenicity

Intraperitoneal and intrapleural studies with asbestos and related compounds have mainly been conducted to investigate the importance of fibre size and shape in the induction of mesotheliomas. The most important information has been provided by 3 groups of investigators: Pott et al., Stanton et al., and Wagner et al., each using different techniques but arriving at basically the same conclusions. Pott et al. injected compounds into the peritoneal cavity of rats. Stanton et al. used glass pledgets containing various compounds embedded in gelatin, which they implanted in rats onto the pleural surface. Wagner et al. used an intrapleural inoculation technique, also with rats.

All 3 groups studied different asbestos types and varieties as well as many other fibrous and granular materials of different sizes. (Fibrous: consisting of needle-like particles with an aspect ratio of > 3:1; granular: consisting of particles with a rounded or amorphous structure). Almost any fibrous material studied had the ability to cause pleural or peritoneal mesotheliomas; granular materials usually had not. A list of fibrous materials that have been reported to produce malignant neoplasms upon intraperitoneal/intrapleural injection or implantation is given in table 10. Asbestos and glass fibre varieties milled or ground to yield shorter fibres invariably resulted in a lower mesothelioma incidence than intact fibres of the same material. The durability of the material was also of some importance: fibrous gypsum, for example, which is highly soluble, did not induce mesotheliomas (Pott and Friedrichs, 1972-cited by IPCS, 1986; Pott et al., 1974a,b; Pott et al., 1976; Pott, 1978; Pott et al., 1986; Stanton and Wrench, 1972; Stanton et al., 1977; Stanton and Layard, 1978-cited by IPCS, 1986; Stanton et al., 1981; Wagner et al., 1973; Wagner et al., 1977; Wagner, 1982; Wagner et al., 1982; Wagner et al., 1984).

Wagner et al. reported a strong relationship between the number of fibres > 5 μm length in inoculated samples and the induction of mesotheliomas in rats

after intrapleural injection. The limit of 5 μm is often used for practical reasons to characterize an asbestos sample, since it is the detection limit of fibres countable by light microscope. However, in these experiments all fibres were counted and characterized very precisely by electron microscope; the length of approximately 5 μm nevertheless appeared to be critical for biological activity. Based on an extensive set of experiments, this group tends to consider fibrous samples consisting exclusively of fibres < 5 μm length as having no carcinogenic potency. In a recent experiment by this group, 2 samples of crocidolite, milled for several hours to yield short fibres, caused 13-15% mesotheliomas, although no fibres > 6.5 μm appeared to be present in the inoculum. Upon the detection of longer fibres in the lungs of exposed animals, the inoculum was carefully reexamined, and some fibres in the longer size range were discovered after all (Wagner et al., 1984). The authors ascribed the mesotheliomas to this small fraction of longer fibres; however, it cannot be excluded that smaller fibres were at least partly responsible for the observed effects.

Stanton et al. statistically correlated tumor probability in their experimental model with the number of fibres present in different fibre size categories. Initially, they did so for 17 different glass fibre varieties (Stanton et al., 1977). These experiments seemed to indicate two fibre size categories associated with a high tumor probability: > 8 μm length (which agrees well with the suggested minimal active fibre length of Wagner et al.) and < 1.5 μm diameter. However, Bertrand and Pezerat (1980) elaborated these results and concluded that it was not allowed statistically to separate fibre length and diameter; tumor probability rather seemed to be a continuous, increasing function of the aspect ratio (length:diameter). Extension of the experiments of Stanton et al. to 72 varieties of asbestos, glass fibre and other materials confirmed this: thin fibres shorter than 8 μm and, to a lesser extent, long fibres thicker than 1.5 μm also had a positive correlation with tumor probability. However, statistical correlations should always be interpreted with great care. The correlation data of tumor probability and fibre size in these experiments are presented in table 11 (Stanton et al., 1981).

Pott et al. also developed a hypothesis, based largely on their own experiments. This hypothesis is illustrated in fig. 2. A fibre with length 20 μm or more and diameter 0.1-0.25 μm is considered to have the highest relative carcinogenic potency (100%), which decreases with a decreasing length and/or an increasing diameter (Pott, 1978). The results of Stanton et al. fit in

remarkably well with this hypothesis. The main difference between this theory and that of Wagner et al. is the absence of a narrow definition of a fibre size that determines whether a fibre is biologically active or not; the carcinogenic potential is rather considered to be a continuous function of fibre size. Fig. 2 demonstrates that, at similar fibre concentrations, the risk calculated by Pott et al. from fibres < 5 μm length will indeed be only a fraction of the risk from longer fibres; at high fibre concentrations however, the carcinogenic potency of short fibres might be considerable.

A decreased intrapleural/intraperitoneal carcinogenic potency was reported for chrysotile from which 80% or more Mg had been removed by acid treatment ("acid-leaching"; Morgan et al., 1977; Monchaux et al., 1981). It is uncertain whether this is caused by changes in fibre size or number (splitting), chemical modification, or other factors (IPCS, 1986). However, although chrysotile in the body may be similarly leached, there is no evidence that chrysotile has a lower carcinogenic potency than other asbestos types: some intraperitoneal/intrapleural studies did indicate a lower, some a higher tumor probablility for chrysotile, others indicated no differences between the asbestos types; in most cases the fibre size distribution was not given, which makes a proper comparison impossible (IPCS, 1986).

Modified chrysotile (treated with $POCl_3$ at high temteratures) also had a lower carcinogenic potency than normal chrysotile after intraperitoneal injection (Maltoni, IARC, 1987).

Fibrogenicity

The results of intrapleural and intraperitoneal studies confirm those of inhalation experiments: shorter fibres, both asbestos and nonasbestos, are less fibrogenic than longer fibres of the same material (NRC, 1984; IPCS, 1986). However, investigations concerning the more precise fibre sizes causing fibrosis are not as extensive as for carcinogenesis. Some investigators believe that asbestos-related lung cancer is always preceeded by a fibrotic condition of the lung (Kuschner, 1982; 1986), others feel that both conditions may exist independently (WHO, 1986). Despite the similarity in the fiber sizes that are apparently involved in carcinogenicity and fibrogenicity, there is as yet no evidence from animal experiments that both processes are directly related.

2.2.4. Summary and conclusions

Oral studies

There are no indications that asbestos causes serious effects in rats after either shortterm or longterm ingestion (Meek and Grasso, 1983; Bolton et al., 1982). The only observed noncarcinogenic effect, which was noted in only a few of the performed studies, was minor cellular damage of the mucosal lining of the gastrointestinal tract (Jacobs et al., 1978; Amacher et al., 1974, 1975; Epstein and Varnes, 1978).

Of the available oral animal carcinogenicity studies with asbestos, many were not quite up to accepted standards. In the studies which were considered adequate, only few statistically significant effects were found, in F344 rats and in Syrian hamsters.

In F344 rats, 1% dietary amosite for lifetime caused an increased incidence of C-cell carcinomas of the thyroid and of mononuclear leukemia, but in males only, and no increased gastrointestinal tumors were observed. The indicated tumor types often occur in this strain (McConnell et al., 1983b). 1% Dietary chrysotile with intermediate range fibres caused an increased incidence of benign neoplasms of the colon after lifetime ingestion. However, in another study, 10% of the same asbestos type in feed did not cause any increase in benign or malignant tumors of the colon (Donham et al., 1980); besides, the benign neoplasms were only observed in males, and were only significant when compared with pooled controls (NTP, 1985). 1% Dietary chrysotile with shortrange fibres and 1% dietary tremolite did not cause any increased tumor incidence after lifetime ingestion (McConnell et al., 1983b; NTP, 1985).

In Syrian hamsters, 1% dietary chrysotile for lifetime caused an increased incidence of adrenal cortical adenomas, but in males only, and no increased gastrointestinal tumors were observed (McConnell et al., 1983a).

Occasionally reported peritoneal mesotheliomas may be suggestive of a carcinogenic effect of ingested asbestos, since this is a very rare type of tumor which has been associated with asbestos in intraperitoneal studies; however, they cannot by themselves be considered as evidence of carcinogenicity.

Treatment of rats and hamsters with known intestinal animal carcinogens in addition to asbestos feeding did not suggest that asbestos is a promoter or cocarcinogen after oral exposure (McConnell et al., 1983a,b; NTP, 1985; Ward et al., 1980).

Summarizing, it can be stated that the available animal feeding studies with asbestos do not demonstrate an increased risk of gastrointestinal tumors in rats and hamsters after ingestion. Other tumors that were sometimes slightly increased were usually also found in untreated animals, and were not increased in other comparable studies; they are therefore not considered to be treatment-related.

Inhalation/intratracheal studies

There is sufficient evidence from experiments with rats, mice, hamsters, guinea pigs and rabbits that all asbestos types are carcinogenic in animals after inhalation (IARC, 1977). The types of tumors most often associated with asbestos exposure in rats and mice are adenomas, adenocarcinomas and squamous-cell carcinomas of the lung, mesotheliomas of the pleura, and occasionally, mesotheliomas of the peritoneum. Animal experiments do not confirm the observations from epidemiological studies that the gastrointestinal tract is involved in asbestos-related carcinogenesis after inhalation.

Important quantitative information was provided by Davis et al. (1978, 1980, IARC, 1987), Reeves et al. (1974), Wagner et al. (1974), and a recent review by the IPCS (1986). Based on this information, the following statements can be made.

- The lung cancer incidence in rats resulting from asbestos inhalation is approximately linearly related to the fibre concentration in air, and to the duration of exposure.
- Mesotheliomas, however, are observed relatively frequently among rats exposed either to low asbestos concentrations, or for only short periods of time (after a long latency period). This suggests that a linear exposure-response relationship is less likely for mesotheliomas. This is in accordance with the observations from human occupational studies, in which mesotheliomas appear to be approximately linearly related to fibre concentration, but exponentially related to the time from first exposure (see 3.2.1.).
- Fibre length, and possibly also fibre diameter, are very important for carcinogenic effects after inhalation, with longer and thinner fibres producing more tumors than shorter and thicker fibres; the different asbestos types can only be compared for their carcinogenic potency after a proper fibre characterization.
- In addition to fibre size and concentration, the durability of fibres may be important. This was indicated by inhalation experiments with manmade mineral

fibres, which were sometimes also able to produce small numbers of lung tumors in rats (NRC, 1984; Wagner, 1982). Chrysotile has been reported to dissolve slowly in the body whereas amphiboles remain intact; however, despite these differences in biological solubility there are no clear indications from animal inhalation experiments that chrysotile has a lower carcinogenic potency than other asbestos types with similar fibre dimensions (see also 5.).

Intratracheal studies with rats have demonstrated a strong synergistic effect of asbestos and cigarette smoke, and of asbestos and chemical carcinogens such as polycyclic aromatic hydrocarbons, in the production of lung tumors but not of mesotheliomas (Shabad et al., 1974; NRC, 1984; IPCS, 1986).

Asbestosis is a characteristic fibrosis of the lungs, which begins as an inflammation-like reaction in and around the terminal bronchioles where fibre-containing macrophages aggregate, and gradually progresses into a diffuse focal fibrosis of the lung interstitium and the pleura. Severe asbestosis causes decreased lung capacity and partial or sometimes even complete obstruction of airways (Begin et al., 1983; Glassroth et al., 1984). This fibrosis develops slowly, but is irreversibly progressing, often even after termination of exposure.

Asbestosis has been reported to occur in all animal species after inhalatory exposure to asbestos (shortterm as well as longterm), and after single or repeated intratracheal asbestos instillation (Reeves et al., 1974; Wagner, 1963; Wehner et al., 1979; Begin et al., 1982, 1983).

As in carcinogenesis, more and longer fibres appear to produce more severe asbestosis (Davis et al., 1978; Reeves et al., 1974; IPCS, 1986). The time from onset of exposure and the duration of exposure are both important factors determining the degree of asbestosis that can be observed in rats (Wagner et al., 1974). Inhalation of high asbestos concentrations at separate occasions may produce more severe asbestosis than more continuous inhalation of lower concentrations, despite similarities in cumulative concentration (Davis et al., 1980).

Nonasbestos fibres may also produce asbestosis in rats. They usually give a lower response than asbestos in similar mass concentrations, but the response appears to be concentration- related (Lee et al., 1981; Wagner, 1982).

The lowest asbestos concentration studied in animals (1 $mg.m^{-3}$ chrysotile, with 99% fibres shorter than 5 μm ; concentration of fibres longer than 5 μm: 3000 $f.l^{-1}$), inhaled for 18 months did not cause any fibrotic reactions in rats

(Platek et al., 1985). However, the same mass concentration with a slightly higher concentration of fibres longer than 5 μm ($1.3x10^{4}f.1^{-1}$) did cause minimal fibrosis in hamsters after 15 months inhalation (Wehner, cited by IPCS 1986). In the latter study, no indication was given of fibre size distribution.

Intrapleural/intraperitoneal studies

Intraperitoneal and intrapleural studies with asbestos and related compounds have mainly been conducted to investigate the importance of fibre size and shape in the induction of mesotheliomas. Three different groups of investigators arrived at basically the same conclusions. Mesotheliomas could be induced in rats by a variety of durable fibrous materials including asbestos by these routes. The tumor probability seems to be a continuous function of both fibre length and fibre diameter, and is relatively independent of the type of material. Fibres with a length of 20 μm or more and diameter 0.1-0.25 μm probably have the highest relative carcinogenic potency, which decreases with a decreasing length and/or an increasing diameter. The risk of fibres with a length of < 5 μm, and of fibres with a diameter of > 2 μm, which may still have some carcinogenic potency (Pott, 1978; Stanton et al., 1981), is assumed to be zero by many investigators (Wagner et al., 1973; Wagner, 1982) and will in any case be negligible in practice.

There are no indications from intrapleural and intaperitoneal studies that chrysotile and the amphiboles differ in carcinogenic potency. However, chrysotile from which more than 80% Mg had been removed by acid treatment (simulating the leaching of chrysotile fibres in the body) had a reduced carcinogenic potency in rats after intrapleural inoculation (Monchaux et al., 1981).

Modified chrysotile (treated with $POCl_3$ at high temteratures) also had a lower carcinogenic potency than normal chrysotile after intraperitoneal injection (Maltoni, IARC, 1987).

The results of intrapleural and intraperitoneal studies confirm those of inhalation experiments with respect to asbestosis: shorter fibres, both asbestos and nonasbestos, are less fibrogenic than longer fibres of the same material (NRC, 1984; IPCS, 1986). However, investigations concerning the more precise fibre sizes causing fibrosis are not as extensive as for carcinogenesis. Some investigators suggest that asbestos-related lung cancer is always preceeded by a fibrotic condition of the lung (Kuschner, 1982;

1986), others believe that both conditions may exist independently (WHO, 1986). Despite the similarity in the fibre sizes that are apparently involved in carcinogenicity and fibrogenicity, there is as yet no evidence from animal experiments that both processes are directly related.

2.3. Reproduction/teratogenicity

Although asbestos has been demonstrated to cross the placenta of rats after intravenous injection (see 1.2.3.), only one study -with mice- concerning possible effects of asbestos on embryonic development has been published. Pregnant mice reveived 1.43, 14.3 or 143 μg/ml chrysotile in drinking water (approximately 0.4, 4 or 40 mg/kg b.w./day) from days 1 to 15 of pregnancy, and were sacrificed at day 18. No maternal effects were observed in any of the groups; the average number of implants was slightly lower for the lowest dosage group, which was not considered to be treatment-related; no effects were observed for any of the other measured parameters (average numbers of resorptions and fetuses, fetal weight, malformations and developmental disturbances -Schneider and Maurer, 1977).

In vitro exposure of mouse blastocytes to 1, 10 or 100 μg/ml chrysotile did not affect the development of the blastula in vitro; however, after implantation of exposed blastula into recipients, a dose-related increase in dead and resorbed fetuses was noted. Fetal weigth, growth and development were not affected. Electron microscopic examination of intact blastula and blastula with removed zona pellucida showed that the zona pellucida effectively protected the blastula from fibre penetration (Schneider and Maurer, 1977).

2.3.1. Summary and conclusions

Although asbestos has been demonstrated to cross the placenta of rats after intravenous injection, only one study concerning possible effects of asbestos on embryonic development has been published. The average number of implants in mice receiving approximately 0.4, 4 or 40 $mg.kg^{-1}$ b.w. chrysotile daily in drinking water during pregnancy was slightly lower for the lowest dosage group, which was not considered to be treatment-related; no other effects were observed. In vitro exposure of mouse blastocytes to 1, 10 or 100 $\mu g.ml^{-1}$ chrysotile did not affect the development of the blastula in vitro but caused a dose-related increase in dead and resorbed fetuses after implantation (Schneider and Maurer, 1977).

2.4. Mutagenicity

2.4.1. Bacterial systems

Chrysotile, crocidolite, amosite and anthophyllite were not mutagenic in the Ames test with Salmonella typhimurium and in Escherichia coli, either with or without metabolic activation (Chamberlain and Tarmy, 1977; Szyba and Lange, 1981). Fibrous Richterite, a natural alkali-rich analogue of tremolite, caused a significantly increased mutation frequency in a reverse mutation test with E. coli CSH50. However, metabolic activation increased the mutagenic activity, whereas the durable fibres are very unlikely to be changed by enzymatic processes; it was therefore assumed that an unknown mutagen was introduced along with the unpurified Richterite sample (Cleveland, 1984).

2.4.2. In vitro mammalian systems

One group of investigators reported a weak mutagenic activity of chrysotile, crocidolite and amosite at the HPRT-locus in Chinese hamster lung cells in culture (at 10 $\mu g/cm^2$)[1]. Mutations were restricted to cells containing asbestos dust, containing cells from other cells by gravitational settling (Huang et al., 1978; Huang, 1979). The effects may therefore have been secondary to cytotoxicity (IARC, 1982), or to increased permeability allowing other mutagens into the cells (Newman et al., 1980, cited by EPA, 1985). The mutagenic action of asbestos at this locus could not be confirmed by other investigators at lower dose levels of 0.1-2 $\mu g/cm^2$ in Syrian hamster embryo (SHE) cells and rat epithelial cells (Newman et al., 1980, cited by EPA, 1985; Oshimura et al., 1984; Reiss et al., 1982, 1983). Mutagenicity at the Na^+-K^+-ATPase locus of SHE cells was also absent after exposure to 1-2 $\mu g/cm^2$ chrysotile or crocidolite in vitro (Oshimura et al., 1984).

Dose-related increases in chomosomal aberrations were reported by various authors, for all examined asbestos types, in SHE cells, Chinese hamster lung cells, Chinese hamster ovary (CHO) cells and human blood lymphocytes in culture. Both structural and numerical changes were noted. Breaks, gaps, fragments, aneuploidy and polyploidy were the changes reported most frequently; dicentrics and exchanges were sometimes also noted (Hesterberg and

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1) Concentrations were expressed as $\mu g/cm^2$ of culture dish, because the asbestos particles settled to the bottom within 1 hour after addition of the suspension.

Barrett, 1985; Huang et al., 1978; Lavappa et al., 1975; Oshimura et al., 1984; Price-Jones et al., 1980; Sincock and Seabrigth, 1975; Sincock, 1977, cited by EPA, 1985; Valerio et al., 1983). Hesterberg and Barrett (1985) observed asbestos fibres within mitotic cells, interacting directly with the chromosomes; it was proposed that this physical interaction of asbestos with chromosomes or with structural proteins of the spindle apparatus might be responsible for structural and numerical changes. In contrast, chromosomal aberrations were not observed in human primary fibroblasts and human lymphoblastoid cells after in vitro exposure to chrysotile and crocidolite, in concentrations similar to those used for CHO cells (10 $\mu g/cm^2$; Sincock et al., 1982).

2.4.3. In vivo mammalian systems

Single oral or intraperitoneal administration of different doses of chrysotile (0.4-400 mg/kg b.w.) did not increase the freqency of micronuclei in bone marrow cells of mice; single oral gavage of 100 or 500 mg/kg b.w. chrysotile did not increase the frequency of chromosome aberrations in bone marrow cells of monkeys (Lavappa et al., 1975). Other in vivo mammalian tests were not reported.

2.4.4. Indicator tests

In vitro mammalian systems

Results of sister chromatid exchange (SCE) assays were equivocal: Livingston et al. (1980) reported a significantly elevated SCE rate in CHO cells exposed to 10 $\mu g/ml$ crocidolite; amosite was less effective; larger chromosomes (> 5 μm) were more sensitive to this effect than shorter ones. Casey (1983) did not observe any increase in SCE rate in CHO-K1 cells, nor in human fibroblasts and human lymphoblastoid cells, at 1-50 $\mu g/ml$ crocidolite, chrysotile, or fine and coarse glass fibres.

Asbestos was reported not to produce unscheduled DNA synthesis (UDS) in human fibroblasts. The tested asbestos concentrations in this experiment were probably low, since other effects (single or double strand breaks) were not found either (no other information available; Hart et al., 1979, cited by EPA, 1985). UDS was also not found in rat hepatocytes after treatment with 1-10 $\mu g/ml$ UICC chrysotile B (Denizeau et al., 1985). Treatment of hamster tracheal explant epithelium with 400 $\mu g/ml$ crocidolite did not increase the incorporation of [^{3}H]thymidine into the cells (Mossman et al., 1984). However,

fibrous erionite did cause increased unscheduled DNA synthesis in both mouse C3H,10T1/2 embryo fibroblasts and human A549 lung cells, at concentrations of 50-200 μg/ml (Poole et al., 1983). The same type of erionite also caused an increased morphological transformation in the former test system with erionite (see 2.4.5.). It is therefore interesting to note that this type of erionite, from Oregon, USA, caused almost 100% mesotheliomas of the pleura in rats after inhalation, whereas the mesothelioma incidence from similar asbestos concentrations was much lower -see 2.2.2.

UICC chrysotile and crocidolite did not cause DNA strand breakage in the alkaline elution assay when applied to cultured hamster tracheal cells (Mossman et al., 1983, cited by EPA, 1985), nor did UICC chrysotile, amosite and crocidolite in human broncial organ cultures (Lechner et al., 1983, cited by EPA, 1985).

In vivo human data

Rom et al. (1983) found a marginal increase in SCE levels in circulating lymphocytes with increasing years of asbestos exposure in a group of 25 asbestos insulation workers after controlling for age and smoking ($p = 0.056$). However, the slight increase in SCE rates in the exposed group compared with a group of 14 non-asbestos-exposed controls, was not significant. After controlling for age and asbestos exposure, the effect of smoking on SCE rates was highly significant for both groups ($p=0.002$). Only the rate of SCE in the longest chromosomes (group A) was significantly associated with both factors (asbestos exposure and smoking), with a significant statistical interaction between the two parameters. These results suggest that the SCE rates in asbestos insulation workers were slightly higher than in non- asbestos-exposed controls, but definite conclusions cannot be drawn because of the confounding effects of smoking.

Patients with asbestos-related malignant mesotheliomas were reported to excrete high levels of breakdown products of tRNA in urine. This is assumed to be caused by an increased turnover rate of tRNA in tumor tissue; it is also observed in some other types of cancer (Borek et al, 1977 and Sharma et al. 1983, cited by Solomon et al., 1985). By measuring these nucleosides in asbestos insulation workers without any clinical signs of malignancy, and in controls, 95% of the subjects could be correctly classified as positively or negatively asbestos- exposed; 10 out of 13 as having normal chest radiographs, and 27 out of 30 as exhibiting alterations in either the lung parenchyma or the pleura, or both (Solomon et al., 1985). This technique might therefore be

used as a new early screening method in persons at high risk of mesotheliomas.

2.4.5. Transformations

In vitro transformations were reported in SHE cells at concentrations of 2-4 $\mu g/cm^2$ for crocidolite, amosite and anthophyllite (DiPaolo et al., 1983), at 2 $\mu g/cm^2$ for chrysotile and crocidolite (Oshimura et al., 1984), and at unknown concentrations of crocidolite (Hesterberg and Barrett, 1984, 1985). Brown et al. (1983) did not find an increase in the number of transformed foci in C3H10T1/2 murine fibroblasts after exposure to 5 $\mu g/ml$ amosite or crocidolite. Fibrous erionite form Oregon, USA, caused increased morphological transformation in mouse C3H,10T1/2 embryo fibroblasts at concentrations > 10 $\mu g/ml$ (Poole et al., 1983).

2.4.6. Synergisitic effects

Simultaneous treatment of various strains of Salmonella typhimurium with asbestos and benzo(a)pyrene (BP) in the Ames test increased the mutation frequency compared to treatment with BP alone. The effect of combined asbestos/BP treatment was further enhanced by metabolic activiation. Treatment with asbestos only had no effect (Szyba and Lange, 1981). Treatment with both asbestos and BP also increased the mutation frequency at the HPRT-locus of adult rat liver epithelial cells, but the carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) did not have any synergistic effect with asbestos (Reiss et al., 1983). Treatment with BP likewise increased morphologic transformation of SHE cells treated with asbestos, whereas UV irradiation did not (DiPaolo et al., 1983). Simultaneous treatment of rat hepatocytes with the mutagen 2-acetylaminofluorene (2-AAF) and UICC chrysotile B did not change the UDS response compared to treatment with 2-AAF alone (Denizeau et al., 1985). Treatment of hamster tracheal explant epithelium with either 400 $\mu g/ml$ crocidolite or < 2.5 $\mu g/ml$ (1 x/week) BP did not increase the incorporation of [^{3}H]thymidine into the cells; simultaneous treatment with both agents caused increased [^{3}H]thymidine uptake into the cells and development of squamous metaplasia (Mossman et al., 1984a).

2.4.7. Summary and conclusions

None of the commercial asbestos varieties had any mutagenic properties in bacterial systems (Chamberlain and Tarmy, 1977; Szyba and Lange, 1981); one natural asbestos variety seemed to be mutagenic in a reverse mutation test

with Escherichia coli CSH50 but this was probably due to contamination (Cleveland, 1984).

In in vitro mammalian systems, all tested asbestos varieties were able to induce chromosome aberrations, which consisted of numerical as well as structural changes, including exchanges (Hesterberg and Barrett, 1985; Huang et al., 1978; Lavappa et al., 1975; Oshimura et al., 1984; Price-Jones et al., 1980; Sincock and Seabrigth, 1975; Sincock, 1977, cited by EPA, 1985; Valerio et al., 1983). These mutagenic lesions may be a direct result of physical interaction of asbestos fibres with chromosomes and/or structural proteins of the spindle apparatus. The transformation of cells, which was also frequently reported after asbestos exposure in vitro, may be directly related to this mechanism (Hesterberg and Barrett, 1985). One report of weak mutagenicity of asbestos in CHO cells at the HPRT-locus (Huang et al., 1978; Huang, 1979) could not be confirmed by various other authors (Newman et al., 1980, cited by EPA, 1985; Oshimura et al., 1984; Reiss et al., 1982, 1983); the reported mutagenic action was probably secondary to cytotoxic damage. Testing of single and double DNA strand breakage in both human and animal organ cultures, and testing of unscheduled DNA synthesis in human fibroblasts (EPA, 1985) and rat liver hepatocytes (Denizeau et al., 1985), also gave negative results. In contrast, a type of erionite that was extremely potent in causing mesotheliomas in rats after inhalation, did cause increased UDS in both murine and human cell lines (Poole et al., 1983).

Only two in vivo mutagenicity studies have been reported, in mice and in monkeys; the results of single oral or intraperitoneal chrysotile administration were negative in both species (Lavappa et al., 1975). Although there is no conclusive evidence of an enhanced SCE rate caused by asbestos in in vitro animal systems (Livingston et al., 1985; Casey, 1983), data from occupationally exposed humans suggest that there is a weak relationship between asbestos exposure and SCE rate, which is greatly increased by cigarette smoking (Rom et al., 1983a). A striking increase in bacterial and in vitro mammalian mutagenicity was also observed after simultaneous treatment with asbestos and benzo(a)pyrene, but not with several other chemical mutagens or with UV irradiation (Szyba and Lange, 1981; Reiss et al., 1983; DiPaolo et al., 1983; Denizeau et al., 1985; Mossman et al., 1984a).

From the above data it can be concluded that, although asbestos does not cause gene mutations, it is able to cause chromosomal damage and in vitro transformation in cells into which asbestos fibres are able to penetrate. This effect is greatly enhanced by the presence of benzo(a)pyrene, and possibly

other polycyclic aromatic hydrocarbons, either in the medium surrounding the cells or adsorbed onto the fibres. Additional mutagenic mechanisms may be involved for the asbestiform mineral erionite, which caused unscheduled DNA synthesis in murine and human cell lines.

2.5. In vitro toxicity

2.5.1. Hemolysis

Various authors have reported that asbestos is hemolytic to blood from humans and various animal species in vitro, with chrysotile being much more potent than the amphiboles. Jaurand et al. (1983) reported a slower rate of hemolysis for amphiboles than for chrysotile, but a very similar final degree of hemolysis in vitro for all asbestos types and quartz. Because of its positively charged surface (due to Mg-ions), chrysotile very probably binds to the negatively charged sialic acid groups of the erythrocyte membrane, with consequent membrane deformations and cell damage. If Mg is leached from chrysotile, or if sialic groups are removed from the erythrocyte membrane, in vitro hemolysis of human blood is markedly reduced (Beck and Tilkes, 1980; Brody et al., 1983; Heppleston, 1984) although Jaurand et al. (1983) found that the rate rather than the extent of hemolysis decreased. Amphiboles have a negative surface charge, and are consequently more liable to bind to positively charged membrane components, like phospholipids and proteins (Brody et al., 1983). Leaching (=magnesium depletion) of amphiboles (see 1.3.1.) enhanced their hemolytic capacity (Light and Wei, 1977; cited by Yano et al., 1984). Fibre size is not expected to be important for this type of in vitro toxicity since it is caused by surface characteristics; in fact, extremely short-fibred chrysotile had a strong hemolytic activity (Pele and Calvert, 1983; Pele et al., 1983). The presence of dipalmitoyl phosphatidylcholin, a major constituent of lung surfactant, reduced the hemolytic capacity of amphiboles, and to a lesser extent, of chrysotile (Beck and Tilkes, 1980).

2.5.2. Cytotoxicity

Asbestos fibres have been reported to be toxic to a variety of mammalian cells in culture, including macrophages and macrophage-like cells, fibroblasts and epithelial cells of the lungs and trachea. Cytotoxicity appears to have two phases, as was described for macrophages (IPCS, 1986): a rapid phase, which is probably caused by direct interactions with the cell membrane as in hemolysis, and a more delayed phase, which may be caused by incomplete phagocytosis (see

2.5.3.) or by other mechanisms once the fibres have been taken up by the cells. Cytotoxicity is usually measured as the inability to form colonies (plating or cloning efficiency) or as increased membrane permeability (leakage of cytosolic enzymes like LDH; staining). An increased membrane permeability may also cause leakage of lysosomal enzymes and toxic cell metabolites (e.g. reactive oxygen intermediates) from the cells, which may be responsible for some pathological processes in vivo.
The cytotoxicity of fibres seems to be related to fibre size, with longer fibres generally being more toxic than shorter fibres of the same variety (Kaw et al., 1982; Beck and Tilkes, 1980; Chamberlain et al., 1982; Tilkes and Beck, 1982), although in one study exactly opposite results were reported (Yeager et al., 1983). Since most asbestos types differ in fibre size distribution, studies investigating differences in response for the various asbestos types are difficult to evaluate. Tilkes and Beck (1982) found no great differences between the toxicity of chrysotile, crocidolite, synthetic fluoramphiboles and glass fibres of similar geometric dimensions.
Normal human tracheobronchial epithelial cells were 10 to 15 times more sensitive to the cytotoxic effects of asbestos than bronchial fibroblasts from the same donor (Haugen et al., 1982).

2.5.3. Phagocytosis

Various cell types involved in in vivo phagocytosis of asbestos fibres have been studied in vitro. Macrophages, fibroblasts, mesothelial cells and epithelial cells of the lung, of different species, are able to incorporate asbestos fibres with a length of approximately < 5 μm and diameter < 3 μm; fibres with a larger diameter are not incorporated; longer fibres are often phagocytized incompletely, which causes local membrane damage with concurrent release of intracellular enzymes, and of toxic cell metabolites like reactive oxygen intermediates, as well as an increased cellular metabolism to compensate for the loss of enzymes (which means a permanent strain for the cells). Phagocytosis seems to be independent of the type of material (chrysotile, amphiboles, glass fibre; Beck and Tilkes, 1980).
Doll et al. (1982a,b) observed that human peripheral blood polymorphonuclear leukocytes had a reduced capacity to produce toxic reactive oxygen intermediates (which is a normal detoxification mechanism within macrophages), and a reduced capacity to phagocytize latex beads, after incubation with all asbestos types. According to the authors, this could not be ascribed completely to cell toxicity. Warheit et al. (1984a,b) found a similarly

decreased capacity for in vitro phagocytosis of rat pulmonary macrophages, both after shortterm inhalation of chrysotile in vivo and after incubation with crocidolite or wollastonite in vitro. Donaldson et al. (1985), however, found an increased production of reactive oxygen intermediates in mouse peritoneal macrophages after in vitro treatment with chrysotile. Although these results are not conclusive, they indicate that asbestos may be able to inhibit the normal phagocytic response of blood and lung macrophages to foreign particles.

2.5.4. Migration of macrophages and leukocytes

During normal phagocytosis, the macrophages release chemotactic factors that attract and stimulate other macrophages as well as leukocytes (Myrvik et al., 1985). Incubation of macrophages with various asbestos types resulted in a decreased release of those factors in vitro (Yano et al., 1984; Rola-Pleszczynski et al., 1984; Myrvik et al., 1985). This release-inhibiting effect was dose- related (Myrvik et al., 1985). Thus, high fibre concentrations may reduce the migration of phagocytizing cells towards inhaled fibres in vivo.

2.5.5. Immune response

A cellular immunoresponse (mitosis of immunocompetent cells, also called blastogenic response) can be induced by treatment of those cells in vitro with concanavalin A, phytohemagglutinin, pokeweed mitogen or other compounds. Intraperitoneal injection of mice with asbestos in vivo yielded peritoneal macrophages that were able to reduce the normal blastogenic response of mouse thymocytes to concanavalin A. However, treatment of mouse peritoneal macrophages with asbestos in vitro did not give them this reducing capacity (Donaldson et al., 1985). Therefore, a possible effect of asbestos on the cellular immunoresponse in vivo is probably mediated by macrophages that have been changed by asbestos via (a) factor(s) outside those macrophages.
In contrast, direct incubation of lymphocytes with asbestos did alter the blastogenic response of those cells to concanavalin A, phytohemagglutinin and pokeweed mitogen. Amphiboles decreased the blastogenic response of human blood mononuclear cells and T- cells; chrysotile did not give consistent results (Barbers et al., 1982; Bozelka et al., 1983a). Other fibres, like glass fibre and mineral wool fibre, were inactive.

These results suggest that asbestos may alter the immunoreactivity of organisms in vivo by direct interaction with lymphocytes, as well as by activation of macrophages by some unknown factor.

2.5.6. Summary and conclusions

Various authors have reported that asbestos is hemolytic to blood from humans and various animal species in vitro, which is an indication of interaction with cell membranes. Chrysotile is more potent than the amphiboles for this effect. Fibre size is not expected to be important here, since the effect is probably caused by surface characteristics (Beck and Tikes, 1980; Brody et al., 1983).

Cytotoxicity of asbestos fibres to a variety of mammalian cells in culture, as measured by the inability to form colonies or by an increased membrane permeability, is related to fibre size. Longer fibres are generally more toxic than shorter fibres (Beck and Tilkes, 1980; Tilkes and Beck; 1982; Chamberlain et al., 1982). The toxicity of asbestos fibres to phagocytizing cells may be caused by incomplete phagocytosis. The resulting increased membrane permeability, resulting in leakage of lysosomal enzymes and toxic cell metabolites from the cells, may be responsible for some of the pathological processes in vivo.

Asbestos fibres appear to reduce the phagocytizing capacity of macrophages in vitro (Doll et al., 1982a,b; Warheit et al., 1984a,b). The migration of phagocytizing cells towards inhaled fibres was also inhibited after exposure to asbestos in vitro (Yano et al., 1984; Rola-Pleszczynski et al., 1984; Myrvik et al., 1985). Thus, the normal clearance mechanism of the lungs for foreign particles may be reduced in vivo by asbestos exposure.

In vitro studies suggest that asbestos may alter the cellular immunoresponse of organisms, both by direct interaction with lymphocytes, and by activation of macrophages (Donaldson et al., 1985; Barbers et al., 1982; Bozelka et al., 1983a).

Although some effects observed in vitro may explain some of the processes in asbestos pathology, it must be stressed that they do not represent the situation in vivo and can only give an indication of the mechanisms involved.

3. EFFECTS ON MAN

3.1. Ingestion

Information about the effects on man of oral asbestos exposure is limited to the results of epidemiological studies that have been performed in areas with high asbestos concentrations in drinking water:

USA

-California -San Francisco Bay area (Kanarek et al., 1980; Conforti et al., 1981; Tarter, cited by Marsh, 1983; Conforti, 1983; Kanarek, 1983; Cooper, 1983)

-Connecticut (Harrington et al., 1978; Meigs, 1983)

-Florida -Escambia County (Millette et al., 1983)

-Minnesota -Duluth (Mason et al, cited by Marsh, 1983; Levy et al., 1976; Sigurdson et al., 1981; Sigurdson, 1983)

-Utah (Sadler et al., 1984)

-Washington -Puget Sound region, Seattle (Severson et al., cited by Marsh, 1983; Polissar et al., 1982; 1983; 1984)

Canada

-Quebec (Wigle et al., 1977)

-Other Canadian areas (Toft et al., 1981; Toft and Meek, 1983; Toft et al., 1984)

Some characteristics of these studies are summarized in table 12. All studies, except the case-control study of Polissar et al. (1983), correlated the incidence or mortality of GI cancer, and sometimes of other cancers, in the indicated geographic area with the estimated exposure to asbestos in drinking water. In most areas, subpopulations with high and low estimated exposure could be identified. Asbestos in drinking water originated from corroding asbestos-cement pipes in the distribution network (Connecticut, Florida, Utah), from contaminated surface water due to natural geological sources (California, Canada, Washington), or industrial/mining wastes (Canada, Minnesota). The studies have been critically reviewed by Marsh (1983), Erdreich (1983) and Toft et al. (1984). The main results, as outlined in those reviews, will be discussed below.

3.1.1. Geographical correlation studies

A general determination of the overall presence or absence of a positive association between the estimated asbestos exposure via drinking water and the

observed cancer mortality or incidence is presented in the tables 13 and 14. The data show that one or more studies have found, for males or females, some positive association for neoplasms of the pancreas(7x)[1], stomach (6x), bronchus/trachea/lungs (4x), esophagus (3x), peritoneum (3x), gall bladder (2x), pleura (2x), kidneys (2x), prostate (2x), small intestine (1x), colon (1x), rectum (1x), brain/central nervous system (1x), thyroid (1x); and leukemia/aleukemia (2x). However, there are many inconsistencies in these findings, even between studies in the same areas, accompanied by a considerable discrepancy in results for males and females, and there are many factors which may account for these inconsistencies.

Some factors are inherent to the study design. All studies except one were geographical correlation studies, which did not include any information on an individual level; location and average duration of residence and average water asbestos content of a certain geographical area were used for an estimation of exposure to asbestos, without corrections for migration, variability in daily water source, and confounding risk factors like occupational inhalatory exposure (Marsh, 1983; Erdreich, 1983). In the Californian studies of Kanarek and Conforti et al., somewhat more refined methods were used than in the other studies; for example, an attempt was made to correct, on a group level, for socio-economic variables. The Canadian studies of Wigle et al. (1977) and Toft et al. (1981) were seriously biased by occupational exposure: substantial proportions of the male labour force were employed in asbestos mining and milling (Toft et al., 1984) which is probably why positive associations were observed in males, but hardly in females. Occupational exposure may also have occurred in California and Connecticut (Marsh, 1983), but positive associations between asbestos ingestion and GI cancers were not limited to males in these areas.

Other factors, varying among the studies (see table 12) were:

-Duration of exposure and observation.

Since asbestos-related cancers have a long expected latency period (20-40 years), the Minnesota, Florida, Connecticut and Utah studies with a relatively short duration of exposure (see table 12) may give less positive associations at this early moment of observation, than at later stages (Erdreich, 1983). In Minnesota, regular updates of the earlier

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1) The number between parentheses indicates the number of studies in which a positive association was found.

investigations of Mason et al. (cited by Marsh, 1983) and Levy et al. (1976) have not (yet) shown significant trends for any effect with time (Sigurdson et al., 1981; Sigurdson, 1983).

-Exposure levels.

In California, where 4 subpopulations with different exposure levels could be identified, the trend of an increasing cancer incidence with increasing exposure level was highly significant in both males and females for combined digestive tract neoplasms and for combined digestive-related organ neoplasms, but not for neoplasms at single sites. The trend for respiratory cancers was highly significant in males only (which might be an indication of higher occupational exposure in residents of areas with high drinking water levels; Kanarek et al., 1980).

Exposure levels in Connecticut, Florida and possibly also Utah were low compared with the other areas (see table 12). Assuming a linear relationship between exposure and effects, the possibility of detecting any carcinogenic effects from asbestos ingestion is therefore lower in these studies than in the other studies, and negative results cannot be extrapolated to possibly higher exposure situations (Marsh, 1983b; Erdreich, 1983). However, since these relatively low exposure levels are probably representative for areas with asbestos cement pipes as the only source of fibers in drinking water, the results may reflect the absence of a risk for general populations in such areas.

-Detection potential.

Erdreich (1983) selected two studies (the California and Washington studies which were valid with respect to the above mentioned factors) to determine if they had the potential to detect the risk that was estimated by the EPA (1980) for asbestos ingestion (based on human inhalatory exposure data; this estimation has now been revised, because new animal ingestion studies have become available). It was concluded that these studies did not have the statistical power to detect such an expected risk. The positive associations found in these studies between asbestos ingestion and cancer of the stomach, esophagus and pancreas (California) and of the small intestine (Washington) can therefore only be considered qualitatively. Probability analysis for each cancer site, using the data from all studies represented in table 12, indicated that the stomach and the pancreas were the sites with the lowest probability of increased cancer by chance only (Marsh, 1983).

3.1.2. Case-control studies

A case-control study in Washington did not reveal any differences in oral asbestos exposure between a group of 382 cancer patients (cancer of the buccal cavity, pharynx, respiratory system, digestive system, bladder or kidneys) and a group of 462 unmatched controls. Asbestos exposure assessment was based on residence, workplace history, smoking and dietary habits, and individual water consumption data. Fitting of all data into a logistic regression model gave positive correlations between cancer at various sites and the major known risk factors (age, smoking habits); the only significant correlation between asbestos ingestion and cancer type was for stomach cancer in males. In females, however, this correlation was negative, which reduces the importance of this finding (Polissar et al., 1983; 1984). Other case-control studies have not been reported.

3.1.3. Summary and conclusions

Geographical correlation studies, relating a high asbestos level in drinking water to the cancer incidence or mortality in a certain region, generally suffered from bias from factors inherent to the type of study, as well as from severe other limitations (Marsh, 1983; Erdreich, 1983). Among the inherent factors was occupational exposure to asbestos (Wigle et al., 1977; Toft et al., 1981), which is probably why positive associations were observed in males but hardly in females in these studies. In many studies the average duration of exposure to asbestos at the moment of observation was shorter than the latency period for asbestos-related cancers (Marsh, 1983; Levy et al., 1976; Sigurdson et al., 1981; Sigurdson, 1983; Millette et al., 1983b; Harrington et al., 1978; Meigs, 1983; Sadler et al., 1984). In some studies the estimated exposure levels were low (Millette et al., 1983b; Harrington et al., 1978; Meigs, 1983; Sadler et al., 1984), which means that negative results cannot be extrapolated to possibly higher exposure situations. However, since these relatively low exposure levels are probably representative for areas with asbestos cement pipes as the only source of fibres in drinking water, the results may reflect the absence of a risk for general populations in such areas.

One series of studies potentially valid with respect to duration and level of exposure and population size (Kanarek et al., 1980; Conforti et al., 1981; Tarter, cited by Marsh, 1983; Conforti, 1983; Kanarek, 1983; Cooper, 1983) was highly suggestive of a positive association between asbestos ingestion and gastrointestinal cancer, with the stomach and pancreas being the least likely

sites to give cancer by chance only. However, these effects may have been the result of occupational or environmental exposure to asbestos, which could not be excluded in this region. Another potentially valid series of studies showed no positive association for these cancer sites (Severson et al., cited by Marsh, 1983; Polissar et al., 1982).
Only one case-control study has been reported; in this study cancer of the digestive tract and related organs did not show a consistent relation with asbestos exposure (Polissar et al., 1983; 1984).
Summarizing, it can be stated that the results of geographical correlation studies, relating asbestos ingestion to cancer incidence or mortality, are not reliable, although some are suggestive of a slightly increased risk of cancer of the stomach and pancreas. Since only one case-control study and no cohort studies are available, no firm conclusions can be drawn. Remarkably, adequate animal carcinogenicity studies are negative with respect to asbestos ingestion (see 2.2.1.).

3.2. Inhalation

Most information on the inhalatory effects of asbestos on man can be derived from occupationally exposed groups; some information is also available from environmental exposure. Detailed reviews of the most important available literature have recently been given by the EPA (1985), the IPCS (1986) and the WHO (1987). The main issues as outlined in these reviews will be discussed below.

3.2.1. Carcinogenic effects

There is sufficient evidence that asbestos is a human carcinogen after inhalation. All five major commercial varieties (chrysotile, crocidolite, amosite, anthophyllite and tremolite) have been linked to excess lung cancer and mesotheliomas of the pleura and peritoneum (EPA, 1985; IARC, 1982; IPCS, 1986; WHO, 1987).

Occupational exposure

The EPA (1985) reviewed 41 large and recent cohort studies of workers exposed occupationally to asbestos during manufacturing (gas masks; textiles; friction products; cement products), mining, or building/construction activities (insulation application; work at shipyards). The studies were listed according to the type of asbestos involved in exposure; however, the cohorts exposed to amosite and crocidolite had usually been exposed to chrysotile also, sometimes

in very considerable concentrations. Data are given in table 15. In the largest study (Selikoff et al., 1979), 922 cases of cancer as a cause of death were recorded among 17,800 insulation workers, against 320 expected, and cancer was thus increased from 19.3% to 43.8% of total mortality. The workers had been exposed to chrysotile and amosite (mixed exposure category). Because of its size, this study is probably the most appropriate to demonstrate the full spectrum of malignant disease from asbestos exposure. More specific data of this study are given in table 16.

Lung cancer (bronchial carcinoma)

As can be seen in table 16, lung cancer in the cohort of insulation workers examined by Selikoff et al. (1979) contributed most to cancer mortality (21% of total mortality). Upon review of all available clinical, surgical and autopsy material there appeared to have been some misdiagnoses: liver cancer secondary to lung cancer was often classified as the cause of death (Selikoff et al., 1979). Since lung cancer is a common form of cancer, similar misdiagnoses are expected in the general population, and a large effect on O/E ratios is therefore not probable.

Of the 41 studies reviewed by the EPA (1985), 30 showed an increased standard mortality rate (SMR) for lung cancer at the 5% level of significance, with SMR ranging from 1.25 to 8.75 (see table 15). The relatively large variability may be the result of different exposures in the different occupational groups, of different fibre types, and of a variety of other factors. All factors will be discussed using the data on exposure-response relationships that were established by the EPA (1985). Before exposure-response relations are discussed, some attention must be paid to the effects of age and of smoking.

-Time-age dependence.

Information on lung cancer risk from exposure at different ages is now available from two studies (Selikoff et al., 1979; Seidman, 1984) in insulation workers, first employed between 15 and 24 years of age, and 25-34 years of age, respectively. Plotting of the relative risk (O/E ratio) of lung cancer against age yielded identical curves with a distance of 10 years. This indicated that the relative risk is relatively independent of the age of first exposure. (The excess risk from asbestos exposure depends on the underlying risk, at zero exposure, which may be determined by many factors, among which cigarette smoking. This excess risk from asbestos exposure increases with age, with the greatest slope for first exposure at older ages; EPA, 1985).

If the data of the two studies are combined, there appears to be a linear increase in the relative risk of lung cancer with years from onset of exposure, with a latency period of approximately 10 years. After 40 years, there is a sudden decrease. The reason for this decrease is not understood; it may be partly related to termination of exposure, relatively earlier deaths of smokers, elimination of asbestos from the lungs, and individual differences in susceptibility. A decrease in relative risk after 35-40 years was also observed by other investigators (EPA, 1985).

-Smoking.

Hammond et al. (1979) investigated the influence of smoking on lung cancer in a large cohort of asbestos workers. During a period of 10 years, beginning 20 years or more after onset of exposure, 299 deaths from lung cancer occurred among 6841 smokers, and 8 among 1379 non-smokers, against 60.9 and 1.5 expected for non-asbestos-exposed smokers and non-smokers, respectively. (The expected data were based on standardized mortality rates in a control group of 73,763 white males exposed to dusts, fumes, gases or chemicals at non-farming work). Both the smoking and non-smoking lung cancer risk appeared to be multiplied approximately 5 times by asbestos exposure. However, smoking by itself caused an increase in lung cancer of approximately 10-11 times, and the risk of asbestos-exposed smokers thus was as much as 50-55 times higher than for non-asbestos-exposed non-smokers.

Other investigators reported similar results, although there was never as exact a multiplicative effect as in the former study. For example, an approximately 25 times increased risk in heavy smokers with high asbestos exposure was found compared to non-smokers with very low asbestos exposure in chrysotile mining (McDonald et al., 1980). The observed increase in mortality from smoking alone, however, was higher in the lower exposure group (11.8x versus 3.6x at high exposure) and the observed increase in mortality from asbestos-exposure alone was higher in non-smokers (6.9x versus 2.1x in smokers).

-Exposure-response relationships.

In 10 studies, lung cancer mortality data have been compared for several subgroups with different estimated cumulative asbestos exposure, thus providing exposure-response information. It must be stressed, however, that the estimation of longterm exposure from total particle count or mass concentrations to fibre concentrations, as measured at separate short-lasting occasions, is very inaccurate.

7 Studies showed a linear relationship between lung cancer mortality and estimated cumulative asbestos exposure (Dement et al., 1983a,b; McDonald et al., 1980; 1983a,b; Henderson and Enterline, 1979), in 2 the relationship was very weak (Seidman, 1984; Finkelstein, 1983) and in 1 the proportion of untraced individuals was too large to give reliable exposure-response information (Weill et al., 1977). However, although the relationship appeared to be linear, the slopes of the 7 given regression lines were different.

The EPA (1985) conducted a new regression analysis of all available studies providing exposure-response information (including the 10 mentioned studies and 4 others: Peto, 1980; Nicholson et al., 1978; Rubino et al., 1977; Selikoff et al., 1979). It was found that a linear relationship between exposure and lung cancer response was likely in these studies. Estimates were made of the fractional increase in lung cancer risk per unit exposure (K_L, the slope of the regression line). Exposure was expressed as cumulative exposure in fibre- year/ml (f-y/ml). Data from all sources within each study were used; adjustments were made where necessary (for details see the EPA report). The results of this extensive analysis are illustrated in fig. 3, which shows the calculated values of K_L and its 95% confidence limits for the 14 studies. The calculated K_L varied roughly between 0.0001 and 0.07/(f-y/ml). In a similar analysis, Liddell and Hanley (1985) arrived at values for K_L ranging from 0.0004 to 0.015/(f-y/ml) (as cited by the WHO- report, 1987). In the WHO-report (1987), a value of 0.01 was adopted as a "best estimate" of K_L.

Although the existence of a linear relationship between exposure and lung cancer response is, in view of the inaccurate estimates of past exposures, not unanimously accepted, it seems to be the most likely and most practical assumption for a quantitative risk assessment (Doll, IARC, 1987).

-Different fibre types

Fig. 3 demonstrates that there is a large variability in K_L as calculated by the EPA (1985) and by Liddell and Hanley (1985), both within and between cohorts exposed to the same type of fibre. The variation may for a large part be due to to methodological limitations in exposure estimates and epidemiological assessment of the response, and to statistical uncertainties associated with a limited number of deaths. Furthermore, fibre size and exposure conditions may differ for various occupational groups (see below). For amosite and for mixed fibre exposure, the values for K_L were comparable to those for chrysotile in the textile production groups (EPA, 1985). Thus,

there is no evidence for differences in lung cancer response between the fibre types.

-Different occupations.

Chrysotile textile production imparts a significantly higher risk per unit fibre exposure than chrysotile mining and friction products manufacturing, although for the latter the uncertainties are greater. This is illustrated in fig. 3. These differences are probably caused by differences in fibre sizes involved in the different occupations: as the -initially long and curly fibred- chrysotile is processed, the percentage of respirable fibres increases (EPA, 1985; McDonald et al., 1984).

-Intermittent versus continuous exposure.

Short, intense exposures, as in some operations (e.g. insulation, maintenance) could have an effect different from longer and lower exposures to the same fibres. However, indirect information (no details; EPA, 1985) suggests that the magnitude of this effect, if present, is less than the variability between studies with continuous exposure. Henderson and Enterline (1979) found that the excess lung cancer risk for plant-wide maintenance mechanics was only slightly higher than that for production workers at the same plant, on a unit exposure basis; insulation workers exhibited similar unit exposure risks as groups with more continuous exposure (EPA, 1985).

Mesothelioma

The study of Selikoff et al. (1979) showed high mortality from pleural and peritoneal mesotheliomas in insulation workers exposed to both chrysotile and amosite. Certified were 25 cases of pleural, 24 cases of peritoneal, and 55 cases of unspecified mesotheliomas. Mesothelioma is a very rare type of tumor, probably causing less than 0.04% deaths in the general USA population (WHO, 1987), and therefore not easily recognized. Re-evaluation of the available information showed that many existing mesotheliomas had been misdiagnosed as pancreatic cancer, liver cancer or unspecified abdominal cancer. The numbers of cases after re-evaluation were 63 for pleural, and 112 for peritoneal mesotheliomas (2.8 and 4.9% of total mortality, respectively).

Pleural mesotheliomas and peritoneal mesotheliomas were found as a cause of death in 30 and 21 of the 41 studies reviewed by the EPA (1985), respectively. Expressed as % of total mortality, the values for pleural mesotheliomas ranged from 0.3 to 1.2% in chrysotile-exposed groups, from 0.3 to 3.1% in groups exposed predominatly to chrysotile, from 1.2 to 1.3% in amosite-exposed

groups, from 1.4 to 7.8% in crocidolite-exposed groups and from less than 0.1% to 8.3% in mixed exposure groups. For peritoneal mesotheliomas, these values ranged from less than 0.1 to 0.4% for chrysotile, from less than 0.1 to 2.4% for predominantly chrysotile, from 0.3 to 1.3% for amosite, from less than 0.1 to 11.3% for crocidolite and from less than 0.1 to 6.9% for mixed exposure. No mesotheliomas were reported in the only investigated group exposed to anthophyllite. However, misdiagnoses as reported by Selikoff et al. (1979) may have led to underestimations of this type of cancer in most studies.

-Time-age dependence.

In the studies of Selikoff et al. (1979) and Seidman (1984), the data on mortality from mesotheliomas in asbestos workers first exposed at ages 15-24 and 25-34, respectively, were roughly parallel, and separated by 10 years. Thus, the absolute risk of death from mesotheliomas appears to be independent of the age at which first exposure occurs (EPA, 1985). (The data for peritoneal and pleural mesotheliomas were combined in this analysis). This was confirmed by Peto et al. (1982) who reviewed the data from 5 cohort studies (Selikoff et al., 1979; Newhouse and Berry, 1979; Peto, 1980; Hobbs et al., 1980; Seidman et al., 1979) with respect to mesotheliomas.

Several authors reported that the relationship between mesothelioma death rates and time from first asbestos exposure was exponential rather than linear, with a delay of several years before the first cases appear:

$$I_M = c.(t-w)^k$$

with I_M = mesothelioma incidence (or death rate), c = an empirical constant (representing, or including, exposure), t = time since first exposure, w = the delay in expression of the risk (probably 10 years), and k = the empirically derived exponent. Peto et al. (1982) found that the data for 20-45 years from onset of exposure in 5 occupationally asbestos-exposed cohorts best fitted the expression using w = 0 and k = 3.2. Earlier mesothelioma death rates, however, were smaller than described by this equation; for all data up to 45 years from onset of exposure, w = 10 and k = 2 fitted better. Subjects exposed before 1922 and after 1946 and over the age of 80 were excluded; if these were included, a value of k = 5 was found to be more appropriate (EPA, 1985; Peto, 1980).

Plotting of the combined data of the studies of Selikoff et al. (1979) and Seidman (1984) showed that mesothelioma death rates in insulation workers

increased with time until 40 years from onset of exposure; at 50^{+} years from onset, a decrease could be observed as in lung cancer (EPA, 1985).

-Smoking.

No relationship was found between cigarette smoking and the risk of death from mesotheliomas (EPA, 1985; Hammond et al., 1979; IPCS, 1986).

-Exposure-response relationships.

From the 14 studies providing exposure-response information for lung cancer, only 4 were considered suitable by the EPA (1985) for a calculation of mesothelioma risk per unit exposure (Selikoff et al., 1979; Peto, 1980; Seidman, 1984; Finkelstein, 1983). For calculation of the mesothelioma risk per year, a linear relationship between unit exposure and risk was assumed, and the intensity and duration of estimated exposure were included in an integration of the mesothelioma/time equation (for further details see the EPA report). The estimates of mesothelioma risk thus obtained were relatively similar for 3 studies and higher for 1; however, there are too many uncertainties to draw conclusions. The ratio mesothelioma risk to excess lung cancer risk was remarkably constant, suggesting that the same factors involved in lung cancer also determine the incidence of mesotheliomas (EPA, 1985).

-Different fibre types

As in lung cancer, it is not possible to separate the effect of mineral type from other factors contributing to the variability found in mesothelioma death rates (EPA, 1985). However, most data are suggestive of a higher general mesothelioma risk after exposure to amphiboles, especially crocidolite, than to chrysotile (IPCS, 1986; IARC, 1987). Recent autopsy studies, in which the lung contents of mesothelioma patients working in different types of asbestos-processing industries were compared, appeared to confirm this. The lungs of chrysotile workers with mesothelioma contained up to 400x more (chrysotile) fibres than the fibres (amphibole) in the lungs of amphibole workers.

Peritoneal mesotheliomas have almost exclusively been associated with amphibole exposure (EPA, 1985).

-Intermittent versus continuous exposure.

Because of the exponential relationship of mesothelioma risk with time, longterm continuous exposure resulting in a certain cumulative fibre dose will very probably give a lower risk of mesotheliomas than exposure to the same cumulative dose in a short period of time. For shortterm exposure, the effects of continuous and intermittent exposure will probably be comparable.

However, there is no direct experimental evidence to support this (EPA, 1985).

GI_cancers

The study of Selikoff et al. (1979) showed a significantly increased mortality from cancer of the esophagus, stomach, and colon-rectum among asbestos insulation workers. Evaluation of 41 studies by the EPA (1985) demonstrated that the increase in GI cancer was usually smaller than that in lung cancer. Therefore, the studies giving no increase in lung cancer are probably not sensitive enough to detect any increase in GI cancer on a statistically significant scale.

In 10 out of 23 occupationally asbestos-exposed cohort studies powerful enough to detect increased GI cancer, an increased risk (expressed as O/E ratio) was demonstrated at the 5% level of significance. The relationship between increased GI cancer risk and increased lung cancer risk is very consistent (EPA, 1985). Because of the lack of confirming animal data and of a dose-response relationship, some authors ascribe the excess GI cancer mainly to misdiagnoses of lung cancer and mesotheliomas (EPA, 1985; IPCS, 1986). Although the EPA Cancer Asessment Group concludes that the evidence for a causal relationship between asbestos exposure and GI cancer is strong (EPA, 1985), the WHO considers the evidence for the induction of gastrointestinal cancers by asbestos weak and states that "the risk to the general population is very small, if any" (WHO, 1987).

A causal relationship between asbestos inhalation and GI cancer cannot be excluded. However, since the magnitude of the excess GI cancer after occupational asbestos exposure is considerably less than for lung cancer, the risk of GI cancer will not have a direct impact on the risk assessment with respect to asbestos inhalation in the general population. It must be stressed that the possible carcinogenic action of asbestos in the GI tract after inhalation does not imply that asbestos acts as a carcinogen after ingestion - see 5.

Other cancers

The study of Selikoff et al. (1979) showed a significantly increased mortality from cancer of the larynx, pharynx/buccal cavity and kidneys. Many other tumors were also increased, but not to a statistically significant degree for individual sites. As a group, all cancers other than those already mentioned were significantly increased (184 observed from best evidence versus 131.8

expected). Of the 41 studies reviewed by the EPA, 1 showed a significant increase in laryngial cancer, and 2 studies, both gas mask manufacturing with predominantly exposure to crocidolite, showed increased cancer of the ovary at a 5% level of significance. Although these data are suggestive, they do not give sufficient evidence of a causal relationship with asbestos exposure.

Non-occupational exposure

There are some indications that the risk of mesotheliomas may be increased for individuals who live near asbestos mines or factories. However, the proportion of recorded mesothelioma patients who live in the vicinity of asbestos mines or factories differs greatly for different areas, and little is usually known about the patients (e.g. about the duration of residence); the results of ecological studies (with asessment of exposure on population basis rather than on an individual level) are often biased by occupational exposure. There are no indications that the risk of lung cancer or other cancers may be increased from neighbourhood exposure. Furthermore, airborne fibre levels near asbestos facilities were generally much higher in the past than they are now (IPCS, 1986).

There are strong indications that household contacts (family, including pet dogs) of asbestos workers have an increased risk of mesotheliomas and lung cancer (Anderson et al., 1976; Glickman et al., 1983; IPCS, 1986). These data appear to be consolidated by the measurements of several times higher fibre concentrations in the homes of chrysotile miners compared with non-miners (Nicholson et al., 1980; IPCS, 1986). However, it must be noted that early day home fibre concentrations used to be higher than concentrations currently allowed in occupational situations; they can therefore not be considered to be low exposure situations.

Direct exposure-response information for very low exposure situations is not available. Mortality data from Canada, the USA, Norway, Finland and the United Kingdom suggest, however, that exposure to "background" levels asbestos (non-occupational exposure, as estimated from the effects in females) does not contribute much to the risk for mesothelioma and lung cancer. Since the start of the industrial application of asbestos in the 50's, when the mesothelioma incidence was low and identical for males and females, the mesothelioma incidence for males has risen steadily, whereas that for females hardly changed during the last 10 to 20 years (McDonald, IARC, 1987).

3.2.2. Noncarcinogenic effects

Asbestosis

Asbestosis is a chronic progressive fibrosis of the lung parenchyma (see 2.2.2.), which may cause shortness of breath and rales as the primary symptoms, and may in severe cases lead to weigth loss and ultimately to death. Asbestosis is characterized radiologically by small irregular opacities, usually on the lower and middle lung fields. In humans, this is often accompanied by evidence of pleural fibrosis or thickening (plaques), as well as pleural calcifications. It is mostly the parietal pleura that is involved, but the visceral pleura may also show lesions. Detection of asbestosis rarely occurs before 20 years from first exposure to asbestos under recent (=not exceptionally high) exposure conditions (IPCS, 1986; EPA, 1985).

Analysis of clinical and X-ray signs of asbestosis according to cumulative exposure in an asbestos textile factory suggested that the risk of developing asbestosis is less than 1 percent from an exposure to 0.7 f/ml for 40 years (= 28 f-y/ml; Berry et al., 1979). However, all individuals in this study were exposed for the first time to asbestos after 1950, and since asbestosis will progress after termination of exposure in the majority of cases, an increasing prevalence with time among this population cannot be excluded. Other analyses among populations of asbestos factories suggested a risk of radiographic abnormalities of less than 2 percent at cumulative exposures of 25 f-y/ml. However, findings of abnormal X-rays, predominantly of the pleura, among family contacts of asbestos workers suggest that very low exposures may produce signs of asbestosis if the time between exposure and observation is long enough (EPA, 1985).

The significance of minor X-ray changes is not clear. They may or may not be associated with decreased pulmonary function, and the association between X-ray changes and cancer risk is equally uncertain. Asbestosis as a cause of death, on the other hand, which is frequently noted among occupationally exposed cohorts (see table 15), was never reported in groups exposed to lower concentrations like family contacts (EPA, 1985).

Asbestosis mortality in heavily exposed workers seems to be related to time sinfirst exposure and to intensity of exposure (IPCS, 1986). However, it is very uncertain if the risk of the generalized progressive condition is linearly related to the intensity of exposure. Therefore, extrapolation of occupational exposure data to low exposure levels is not possible. The above observations indicate that asbestosis at low levels of exposure is not

expected to be an important problem; the primary risk consideration at those concentrations is cancer rather than non- malignant disease (EPA, 1985; IPCS, 1986).

3.2.3. Summary and conclusions

Carcinogenic effects

There is sufficient evidence that asbestos is a human carcinogen after inhalation. All five major commercial varieties (chrysotile, crocidolite, amosite, anthophyllite and tremolite) have been linked to excess lung cancer and mesotheliomas of the pleura and peritoneum (EPA, 1985; IARC, 1982). Of 41 occupationally asbestos-exposed cohort studies reviewed by the EPA (1985), 30 showed an increased standard mortality rate (SMR) for lung cancer at the 5% level of significance, with SMR ranging from 1.25 to 8.75. The relatively large variability may be the result of different exposures in the different occupational groups, of different fibre types, and of a variety of other factors. Mortality from pleural mesotheliomas occurred in 30 of the 41 studies (in 23 out of the 30 studies that were significantly positive for lung cancer). Mortality from peritoneal mesothelioma occurred in 21 of the 41 studies (in 19 out of the 30 studies that were significantly positive for lung cancer). However, many peritoneal mesotheliomas may have been misdiagnosed as pancreatic or other cancers (Selikoff et al., 1979). See also the table in this paragraph.

The relative lung cancer risk from asbestos exposure (observed/expected) appears to be independent of age. The excess risk (observed - expected) for mesothelioma (which is considered to be equal to the absolute risk, since the incidence in the general population is very low) is also independent of age. However, the excess risk for lung cancer linearly increases with age. The relative risk for lung cancer is approximately linearly increased with the time from onset of exposure, with a latency period of approximately 10 years, whereas the risk for mesotheliomas is rather exponentially increasing with the time from first exposure to asbestos. However, at 40-50 years after onset of exposure, there is a sudden decrease for both lung cancer and mesothelioma, which is only partly understood (Selikoff et al., 1979; Seidman, 1984; EPA, 1985).

Both lung cancer and mesothelioma risk are probably linearly related to the asbestos fibre concentration in air. In most cohort studies, however, fibre concentrations were not measured directly, but calculated from mass or total

particle count measurements. Therefore, the intensity of exposure to fibres, as given for these studies, can only be a rough estimate. Whereas some investigators feel that the existence of a linear relationship between fibre concentration and tumor incidence is only speculative, and that quantitative risk estimates based on these inaccurate data are not possible (IPCS, 1986; IARC, 1987), others nevertheless applied linear regression models to describe the relationship between the observed mortality from lung cancer in the various cohorts and the estimated cumulative exposure (Liddell and Hanley, 1985; EPA, 1985). During a recent IARC symposium it was reconfirmed that, despite all possible objections, a linear non-threshold extrapolation model seems to be the most appropriate model for a quantitative risk assessment of asbestos (Doll, IARC, 1987).

Mortality from mesotheliomas in 41 cohort studies (EPA, 1985).

Fibre type	Number of studies	Mortality[1], % of total mortality (n= number of studies with mesotheliomas > 0)	
		Pleural mesotheliomas	Peritoneal mesotheliomas
Chrysotile only	9	0.3-1.2% (4)	0.2-0.4% (2)
Predominantly chrysotile	6	0.3-3.1% (6)	0.5-2.4% (4)
Amosite	2	1.2-1.3% (2)	0.3-1.3% (2)
Predominantly crocidolite	5	1.4-7.8% (5)	0.9-11.3% (5)
Mixed asbestos	16	0.6-8.3% (12)	3.5-6.9% (8)
Anthophyllite	1	-	-
Talc (with tremolite)	2	-	0.9% (1)

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1) In populations without known asbestos exposure the mortality from mesotheliomas is very low (less than 0.04% of total mortality in the general population of the USA).

The effects of asbestos exposure and smoking appear to be approximately multiplicative. The number of deaths from lung cancer in a large cohort of asbestos workers, for example, was approximately five times higher than expected for both smokers and non-smokers; since smoking by itself caused approximately 10-fold increase in lung cancer mortality, the mortality from lung cancer in asbestos-exposed smokers was 50 times higher than in non-asbestos-exposed non-smokers (Hammond et al., 1979). No effect of smoking was observed for mesotheliomas.

There is no evidence for differences between the different asbestos types with respect to the lung cancer response (EPA, 1985). However, the data from cohort studies suggest that with respect to mesothelioma the amphiboles, especially crocidolite, are more potent than chrysotile (see the table in this paragraph). This appears to be confirmed by data from recent studies with lung autopsy material from mesothelioma patients. The lungs of mesothelioma patients who had been working in the chrysotile industry contained on average 400x more (chrysotile) fibres than the amount of (amphibole) fibres in the lungs of patients working previously in the amphibole-processing industry (Churg and Wright, IARC, 1987).

In 10 out of 23 occupationally asbestos-exposed cohort studies powerful enough to detect increased gastrointestinal cancer, an increased risk (expressed as O/E ratio) was demonstrated at the 5% level of significance. The relationship between increased gastrointestinal cancer risk and increased lung cancer risk is very consistent (EPA, 1985). Because of the lack of confirming animal data and of a dose- response relationship, some authors ascribe the excess gastrointestinal cancer mainly to misdiagnoses of lung cancer and mesotheliomas (EPA, 1985; IPCS, 1986). Although the EPA Cancer Assessment Group concludes that the evidence for a causal relationship between asbestos exposure and gastrointestinal cancer is strong (EPA, 1985), the WHO considers the evidence for the induction of gastrointestinal cancers by asbestos weak and states that "the risk to the general population is very small, if any" (WHO, 1987).

A causal relationship between asbestos inhalation and gastrointestinal cancer cannot be excluded. However, since the magnitude of the excess gastrointestinal cancer after occupational asbestos exposure is considerably less than for lung cancer, the risk of gastrointestinal cancer will not have a direct impact on the risk assessment with respect to asbestos inhalation in the general population. It must be stressed that the possible carcinogenic

action of asbestos in the gastrointestinal tract after inhalation does not imply that asbestos acts as a carcinogen after ingestion -see 5.

Other tumors were sometimes slightly increased in occupationally exposed cohorts but there is no evidence for a causal relationship with asbestos (EPA, 1985; IPCS, 1986).

There are strong indications that household contacts (family, including pet dogs) of asbestos workers have an increased risk of mesotheliomas and lung cancer (Anderson et al., 1976; Glickman et al., 1983; IPCS, 1986). These data appear to be consolidated by the measurements of several times higher fibre concentrations in the homes of chrysotile miners compared with non-miners (Nicholson et al., 1980; IPCS, 1986). The risk of mesotheliomas was also found to be increased for individuals who live near asbestos mines or factories (IPCS, 1986). However, it must be noted that early day home fibre concentrations used to be higher than concentrations currently allowed in occupational situations; they can therefore not be considered to be low exposure situations.

Direct exposure-response information for very low exposure situations is not available. Mortality data from Canada, the USA, Norway, Finland and the United Kingdom suggest, however, that exposure to "background" levels asbestos (non-occupational exposure, as estimated from the effects in females) does not contribute much to the risk for mesothelioma and lung cancer. Since the start of the industrial application of asbestos in the 50's, when the mesothelioma incidence was low and identical for males and females, the mesothelioma incidence for males has risen steadily, whereas that for females hardly changed during the last 10 to 20 years (McDonald, IARC, 1987).

Asbestosis

Analysis of clinical and X-ray signs of asbestosis according to cumulative exposure in an asbestos textile factory suggested that the risk of developing asbestosis is less than 1 percent from an exposure to 0.7 $f.ml^{-1}$ for 40 years (= 28 $f\text{-}y.ml^{-1}$; Berry et al., 1979). Other analyses among populations of asbestos factories suggested a risk of radiographic abnormalities of less than 2 percent at cumulative exposures of 25 $f\text{-}y.ml^{-1}$ (EPA, 1985).

The significance of minor X-ray changes is not clear. They may or may not be associated with decreased pulmonary function, and the association between X-ray changes and cancer risk is equally uncertain. Asbestosis as a cause of death, on the other hand, which is frequently noted among occupationally exposed cohorts, was never reported in groups exposed to lower concentrations

like family contacts (EPA, 1985). Asbestosis mortality in heavily exposed workers seems to be related to time since first exposure and to intensity of exposure (IPCS, 1986). However, it is very uncertain if the risk of the generalized progressive condition is linearly related to the intensity of exposure. Therefore, extrapolation of occupational exposure data to low exposure levels is not possible.

The above observations indicate that asbestosis at low levels of exposure is not expected to be an important problem; the primary risk consideration at those concentrations is cancer rather than non- malignant disease (EPA, 1985; IPCS, 1986).

4. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

4.1. Toxicity to aquatic organisms

Batterman and Cook (1981) determined chrysotile burdens in salmonids that had histories of asbestos exposure. Arctic char (Salvelinus alpinus) from Deception Bay, Canada, had 2.9 and 230.5 f/mg in muscle and kidney tissue, respectively, whereas the fiber concentration in water was 6.7×10^8 f/l (Batterman and Cook, 1981; cited in Belanger et al., 1986 and EPA, 1980).
Ecopathological studies on the effects of asbestos in aquatic organisms have not been performed in a systematic fashion. Black et al. (1982) described mesothelioma, a tumor type frequently associated with asbestos exposure in mammals, in walleye (Stizostedion vitreum) exposed to copper tailings that probably contained asbestos (Black et al., 1982; cited by Belanger et al., 1986). Other studies with asbestos in aquatic organisms have mostly been performed under laboratory conditions.

4.1.1. Algae

Cryptomonas erosa is a representative planktonic alga, commonly found in the Great Lakes area of the USA. Incubation of 5 ml Cryptomonas stock with 5 ml chrysotile asbestos solution (final concentration $1\text{-}1.5 \times 10^6$ f/l) for 72 hours resulted in the detection by TEM (transmission electron microscope) of asbestos fibers, especially smaller fibers, within Cryptomonas cells: in starch deposits, chloroplasts and ejectosomes. There was no evidence for phagocytosis or pinocytosis (Lauth and Schurr, 1984).

4.1.2. Molluscs

Halsband (1974) exposed mussels (Mytilus sp.) to high concentrations of chrysotile (1-100 mg/l) for 10 days, which resulted in accumulation of fibers in intestinal lining tissue. The fibers were not excreted when the mussels were subsequently placed in clean water (Halsband, 1974; cited in Belanger et al., 1986).
Asian clams (Corbicula sp.) were exposed to suspensions of chrysotile asbestos at 0, 10^4 and 10^8 f/l for 96 hours, with and without food, respectively. Siphoning activity (measured as the frequency of shell opening) was observed at 0, 0.5, 1, 2, 4, 8, 24, 48, 72 and 96 hours. The infiltration of asbestos fibers into gill tissue, visceral tissue and whole clam homogenate was examined by TEM after termination of exposure. Compared to untreated controls, the siphoning activity was significantly reduced within 8 hours in clams to

which no food was offered, at all asbestos concentrations alike; in clams to which food was offered, however, asbestos had no effect upon siphoning activity. Asbestos fibers were only found in whole clam homogenate of clams that had been offered food (69 f/mg dry tissue) at the highest asbestos concentration of 10^8 f/l (Belanger et al., 1986).

The experiments with Corbicula sp. where food was offered were extended to 30 days. Clams were observed once daily after feeding, and growth was determined by measuring shell growth and weight. At termination of exposure, visceral and gill tissues were examined by TEM. Siphoning activity was depressed in all asbestos-exposed groups alike, with a correspondingly decreased shell growth. Asbestos fibers were only found at the highest asbestos exposure of 10^8 f/l; 147 f/mg dry tissue was found in gills and 904 f/mg dry tissue in visceral tissue, with the average length of fibers in tissues being smaller than of those in water. Gill tissue appeared to be significantly altered after exposure to 10^8 f/l, with significantly more locules (fluid- filled open spaces between cells) in each lamella than for controls (Belanger et al., 1986).

During 14 days exposure to 10^2 to 10^8 f/l chrysotile asbestos, the larval release pattern of Corbicula sp. was studied. Exposure to asbestos seriously repressed the release of larvae in a dose-related way with no threshold level; larval mortalily increased with asbestos concentration (Belanger et al., 1986).

4.1.3. Fish

Belanger et al. (1985) exposed larvae of the coho salmon (Oncorhynchus kisutch) to 10^6 f/l chrysotile for 40 to 80 days. Lethargic behavior, epidermal hypertrophy, hyperplasia and selective vacuolation near the branchial region, and degradation of the lateral line system were noticed. Mortality was not observed (Belanger et al., 1985; cited in Belanger et al., 1986).

The Amazon molly (Poecilia formosa), a gynogenetically reproducing, live-bearing fish native to Texas, USA, was exposed for 6 months to several concentrations of coarse and fine chrysotile asbestos suspensions in a static test. (Coarse: all fiber sizes, concentrations 0.1, 1 and 10 mg/l; fine: mostly smaller fibers of 0.2-2 μm length, concentrations 0.01, 0.1 and 1.0 mg/l). (According to Cunningham and Pontefract (1973), 1 mg/l asbestos would be 10^{10} f/l; however, it must be stressed that this is only a very rough estimate since the mass:fiber ratio highly depends on fiber size). At the end

of this period, the fish were serially sectioned and the tissues examined for lesions. The kidneys were the major sites of accumulation of the fibers after their entry into the body through the intestinal mucosa. The accompanying table shows the numbers of fish with lesions of the gills and kidneys.

Numbers of surviving Amazon mollies showing lesions of the kidneys and gills after a 6-month exposure to various concentrations of chrysotile asbestos (Woodhead et al., 1983).

Asbestos (mg/l)	Kidney damage	Gill lesions
Coarse suspension		
0.1	4/17	8/17
1.0	5/15	13/15
10	4/14	13/14
Fine suspension		
0.01	0/20	0/20
0.1	12/20	2/20
1.0	17/17	5/17
Controls		
0	1/18	3/20

The number of animals with kidney lesions was greatest in the groups exposed to the finer particles, the probable reason for this being the preferential uptake of smaller fibers by the intestinal mucosa. Pathological changes in the kidneys were: selective necrosis of the hemopoietic tissue, fibrosis, and dilatation of tubules. The injury to the tissue may have resulted from the physical presence of fibers or from their chemical composition (magnesium). Small asbestos fibers would be expected to be easily taken up through the gills, and larger fibers to stay on the outer gill surface; this would explain the higher incidences of gill lesions that were observed in the groups exposed to coarse asbestos suspensions. However, there was no evidence of the entry of particles of any size through the gill epithelium. Nevertheless, epithelial hypertrophy and secondary lamellar telangiectasia of the gills, observed mainly in the groups exposed to coarse asbestos suspensions, appeared to be the result of external irritation of their surfaces by the asbestos particles.

There was no cellular injury in the liver or the muscles (Woodhead et al., 1983).

4.1.4. Summary

The impact of asbestos on aquatic life has largely been ignored. The few studies that are available -mainly laboratory studies- indicate that asbestos fibres are taken up by algae, molluscs and fish, and are able to cause morphological changes in those organs of fish that are involved in the uptake and concentration of fibres from water (gills, kidneys) at relatively high concentrations (10^8 $f.l^{-1}$; Laut and Schurr, 1984; Woodhead et al., 1983; EPA, 1980). In one study, asbestos was shown to affect the growth and reproduction of clams at lower concentrations, from 10^2 to $10^4 f.l^{-1}$ onwards (Belanger et al., 1986). The paucity of the data does not permit any conclusions about the possible effects of asbestos on environmental systems.

5. EVALUATION

The critical effect of asbestos for the general population is cancer.
The results of animal experiments with oral exposure to high concentrations of asbestos fibres are essentially negative. Results of human epidemiological studies relating asbestos exposure via drinking water to health effects are in some cases negative, in some cases there is a suggestion of an increased incidence of gastrointestinal tumors. However, there is a strong possibility of occupational or environmental exposure to asbestos in these studies which may well account for the positive correlations found.
Human occupational studies, in which exposure to asbestos has mainly been inhalatory, sometimes suggest an increased risk of gastrointestinal cancer. Although the evidence must be considered weak (animal inhalation studies did not confirm this risk, and some investigators attribute it to misdiagnoses of peritoneal cancers), a true causal relationship between gastrointestinal cancer and asbestos inhalation cannot be completely excluded. The possibility that asbestos may act as a gastrointestinal carcinogen after inhalation, however, does not necessarily imply a similar carcinogenic action after ingestion because of the differences in dimensions, concentration, and therefore of biokinetics and biological activity of the different fibres involved.
Because the evidence that asbestos may be carcinogenic by the oral route is very weak, the possible risk of cancer caused by ingested asbestos at the current exposure levels is considered neglectable. Therefore, a health based limit value for asbestos in food and drinking water is not proposed.

Inhalatory exposure to asbestos has been associated with cancer. Both from animal studies and human epidemiology there is adequate evidence that inhalation of asbestos may result in lung cancer and mesotheliomas. In some human occupational studies, an increased risk of gastrointestinal cancer was also indicated, but this was always considerably less pronounced than the risk of lung cancer. For a risk assessment, lung cancer and mesotheliomas may therefore be considered as the critical effects of asbestos inhalation.
The risks of lung cancer and mesothelioma have to be assessed separately because of the different exposure-response relations. Lung cancer is approximately linearly related to the duration and intensity of exposure, whereas mesothelioma appears to be related linearly to fibre concentration but exponentially to the time from onset of exposure.

The carcinogenic potency of asbestos appears to be a function of the fibre dimensions which may vary for the different types and brands of asbestos, depending on origin, application, type of processing etc. There is no evidence from inhalation and intrapleural/intraperitoneal animal experiments that chrysotile and the various amphiboles differ in carcinogenic potency as long as they have similar fibre dimensions and concentrations. On the other hand, mesotheliomas are less frequently noticed in epidemiological studies with mainly exposure to chrysotile asbestos, compared with studies in which the exposure was to amphiboles or mixed asbestos. The differences between animal and human data may partly be explained by the (slow) solubility of chrysotile in the tissues (whereas amphibole fibres accumulate in the perifery of the lungs and the pleura), which would account for a lower expression of the carcinogenic potency of chrysotile in humans compared to much shorter-living laboratory animals. However, it may not be possible to compare epidemiological data from different types of industry involving asbestos fibres of completely different dimensions. Fibre dimensions were not given in any of these studies. The results of recent autopsy studies are therefore important: these studies, with lung autopsy material from mesothelioma patients who had been working in different asbestos-producing and processing industries, confirmed that chrysotile may induce mesotheliomas, but in much larger fibre concentrations than the amphiboles. Doll and Peto (1985; IARC, 1987) suggested as a working hypothesis a 20x lower potency to induce mesotheliomas for chrysotile than for the amphiboles. With respect to the induction of lung cancer chrysotile and the amphiboles do not appear to differ.

A broad range of fibres can be inhaled, the upper limits of respirability being approximately 200 μm fibre length and 3 μm fibre diameter. Strictly spoken, "safe" fibre dimensions within the limits of respirability cannot be given, because carcinogenicity is considered to be a continuous function of fibre length and diameter. However, in practice the risk of fibres shorter than 5 μm will be neglectable.

Since no direct exposure-response information is available for very low exposure situations, the risk evaluation will be based on epidemiology from occupationally exposed humans.

Workplace fibre concentrations were usually not measured, but estimated from mass or total particle count measurements, with calibration methods using an optical microscope (OM) for which the detection limits are approximately 5 μm fibre length and 0.3 μm fibre diameter. The risk estimates in this evaluation will thus be based on optically visible fibres. However, fibres present in the

envionment generally have smaller diameters. Since fibres with a diameter of 0.1 to 0.2 μm are considered as the most critical, environmental fibre concentrations have to be measured by electron microscope (EM). To compare OM and EM concentrations a conversion factor has to be used; a factor 2 seems realistic for conversion of workplace to environmental situations (WHO, 1987; Cherrie, IARC, 1987).

The risk for lung cancer is approximately 10 times higher for smokers than for non-smokers, and is approximately multiplicative to the lung cancer risk from asbestos exposure. The risk for mesotheliomas is not influenced by smoking. Since so many uncertainties are involved in a quantitative risk assessment for asbestos, resulting in a broad range of possible risks, it is not considered scientifically appropriate to calculate a separate risk figure for non-smokers in the general population. The risk assessment as given in this document applies to the average general population with approximately 30% smokers.

A detailed description of the risk assessment in the WHO Air Quality Guidelines (1987) was given in a WHO working document (Appendix I of this chapter). The above mentioned risk assessment will be adopted in this Integrated Criteria Document, with modifications.

In the WHO Guidelines, an extra lung cancer risk was given in the range of 10^{-6} to 10^{-5}, and a mesothelioma risk was given in the range of 10^{-5} to 10^{-4} for lifetime exposure to 500 optically visible fibres per m^3, for all asbestos types, for an average population with 30% smokers. In this Integrated Criteria Document, an order of magnitude of 10-100 will be applied for the difference between chrysotile and amphibole asbestos with respect to mesotheliomas, and the ranges of risk given by the WHO Guidelines will be translated into ranges of fibre concentrations that can be associated with lifetime risks of 10^{-6} and 10^{-4}, respectively.

Risk assessment for the general population

Effect	Lifetime risk	Lifetime exposure: Optically measured fibres.m^{-3}	Lifetime exposure: Fibres.m^{-3} longer than 5 μm measured by EM[1].
Mesothelioma (for smokers and nonsmokers)	$1/10^6$	5-50 (amphiboles)	10-100
	$1/10^6$	50-5000 (chrysotile)	100-10,000
	$1/10^4$	500-5000 (amphiboles)	1000-10,000
	$1/10^4$	5000-500,000 (chrysotile)	10,000-1000,000
Lung cancer (population with 30% smokers)	$1/10^6$	50-500	100-1000
	$1/10^4$	5000-50,000	10,000-100,000

It must be stressed again that the figures as given in this table only give a rough approximation of the possible risks, but in general the assessment is believed to be conservative for the protection of health.

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1 Calculated with a conversion factor of 2.

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Table 1. Asbestos fiber penetration into the gastrointestinal mucosa of rats

Route of administration	Daily dose (mg/kg bw)	Type of fiber	Duration	Recovery period	Tissues examined	Analysis	Results(EM) Control	Test	Author(s)
Diet	5000	chrysotile	2 years	1 month	colon	EM	3/240(16)*	6/150(10)*	Donham et al., 1980.
Diet	3000	?	3 months	-	colon	EM	not examined	+	Westlake et al., 1965
Diet (in margarine)	100	chrysotile, crocidolite or amosite	1 year	1 month	intestines	EM	-	1/180(6)*,**	Bolton and Davis, 1976
Diet (in margarine)	100	chrysotile, crocidolite or amosite	2 weeks-1 year	?	intestines	EM	-	-	Bolton and Davis, 1976
Intra-oesophagal (in corn oil)	250	amosite	5 days	1 night	duodenum	PLM, biological effects	-(PLM)	-(PLM)	Meek, 1983; Meek and Grasso, 1983
Intraintestinal (closed cannula; in saline)	appr. 20 (10^{11} fibers of 0.05-25 um length)	amosite	1 hour	-	jejunum	EM	-	+	Storeygard and Brown, 1977

*) Fibers/samples, number in parentheses is number of animals examined

**) Statistical analysis indicated that the amount of fibers penetrating the total gut was, with a probability of 90%, less than 1500 for chrysotile, 550 for crocidolite and 100 for amosite

- = negative
+ = positive, not quantified
? = not reported
EM = electron microscope
PLM = polarizing light microscope

Table 2. Fiber migration from the gastro-intestinal lumen of animals into tissues, organs and fluids outside the gastro-intestinal tract

Route of administration	Calculated daily dose (mg/kg b.w.)	Duration	Cumulative calculated fiber dose (f/g b.w.)	Type of fiber	Recovery period	Tissues examined	Calculated recovery rate **	Analysis	Results(EM) Control	Test	Author(s)
Rat											
Diet (in margarine)	100 or 100 or 100	25 months	7.6×10^{11} " "	amosite crocidolite chrysotile	until natural death	lungs, liver, spleen, kidney, gut, mesentery, omentum, peritoneal wall, thoracic wall	1.7×10^{-10}	EM	not examined	calculated approximate fiber burden/rat: 3000 amosite, 4500 crocidolite, 52000 chrysotile; % outside g.i. tract: 49/55/67	Bolton et al., 1982
Diet (in corn oil or molasses)	500 of 0.3-50 um fiber length 20% > 5um	6 weeks	2.1×10^{11}	chrysotile	-	blood, omentum, lung, kidney, liver, brain	-	EM	+ (except blood)	lung, kidney and brain fiber concentration sign. elevated	Cunningham et al. 1977
Gavage (in suspension)	50 (2x/week); 65% > 10 um length	lifetime*	1.0×10^{11}	chrysotile	-	kidney cortex	1.3×10^{-11}	EM	0.2 fibers/gram dry tissue	5.3 fibers/gram dry tissue in 17 out of 20 rats	Patel-Mandlik and Millette, 1983a,b
In oleo-margarine	1000-2000	6 days	6.0×10^{10} - 1.2×10^{11}	amosite	1,2,3,4, 5 weeks	mesentery, kidney, lung	6.3×10^{-12}	EM	+ (no amosite)	+ (amosite in mesentery, lung); some non-amosite	Gross et al., 1974

Table 2. (continued)

Route of administration	Calculated daily dose (mg/kg b.w.)	Duration	Cumulative calculated fiber dose (f/g b.w.)	Type of fiber	Recovery period	Tissues examined	Calculated recovery rate	Analysis	Results(EM) Control	Test	Author(s)
										contamination; total tissue fiber burden 50 fibers/rat	
In margarine	125 + 0.025-125	1 month + 1xsingle	3.8×10^{10} + 2.5×10^{5} - 1.3×10^{9}	chrysotile	1-48 hours	hepatic portal blood	-	EM	+ (only fibers < lum length)	blood fiber count sign. elevated at most time intervals after single dosage; peak at 7 hours (only fibers < lum length)	Weinzweig and Richards, 1983
Intra-oesophagal (needle)	1000	single	1.0×10^{10}	amosite	48 hours	mesentery, kidney, lung	0	EM	+	only in tissues of 1 animal with perforated oesophagus	Gross et al., 1974
Diet	500	3 hours-12 days	7×10^{8} - 6×10^{10}	chrysotile (shortrange fibers)	-	lymph	0 - 2×10^{-6}	EM	0	13 out of 15 animals positive	Sebastien et al. 1980
Diet	500	3 hours-12 days	4×10^{7} - 4×10^{8}	chrysotile (intermediate range fibers)	-	lymph	0 - 2×10^{-4}	EM	0	4 out of 8 animals positive	Sebastien et al. 1980

Table 2. (continued)

Route of administration	Calculated daily dose (mg/kg b.w.)	Duration	Cumulative calculated fiber dose (f/g b.w.)	Type of fiber	Recovery period	Tissues examined	Calculated recovery rate	Analysis	Results(EM) Control	Test	Author(s)
In gelatin capsule	60-120	single	$7\text{-}14\times10^{8}$	chrysotile	-	lymph	7×10^{-7} - 3×10^{-5}	EM	0	all 5 animals tested were positive	Sebastien et al., 1980
In gelatin capsule	50-150	single	$3\text{-}8\times10^{8}$	crocidolite	-	lymph	0 - 6×10^{-7}	EM	0	3 out of 5 animals were positive	Sebastien et al., 1980
In margarine	0.025-125	single	2.5×10^{5} - 1.3×10^{9}	chrysotile	1-48 hours	hepatic portal blood	-	EM	+ (only fibers < 1um length)	blood fiber count sign. elevated at 7 hours after single dosage of 125 mg/kg (only fibers < 1um length)	Weinzweig and Richards, 1983
Intragastric injection after laparotomy	appr. 25 (10^{11} fibers of 0.5-2 um length)	single	2.5×10^{8}	chrysotile	4 days	blood, spleen, omentum, lungs, brain, heart	1×10^{-3}	EM	+ (except blood)	blood concentration 0.29×10^{6} fibers/gram = sign. elevated; conc. in omentum considerably but not sign., other conc. slightly but not sign. elevated	Cunningham and Pontefract, 1973; Pontefract, 1974

Table 2. (continued)

Route of administration	Calculated daily dose (mg/kg b.w.)	Duration	Cumulative calculated fiber dose (f/g b.w.)	Type of fiber	Recovery period	Tissues examined	Calculated recovery rate	Analysis	Results(EM) Control	Test	Author(s)
Intragastric injection after laparotomy	appr. 2 (10^{10} fibers of 0.5-2 um length)	single	$2.5x10^{7}$	chrysotile	2 days	blood, spleen, omentum, lungs, brain	0.2	EM	+ (except blood)	blood concentration $4.6x10^{6}$ fibers/gram = sign. elevated; other conc. slightly but not	Cunningham and Pontefract, 1973; Pontefract, 19
Baboon Gavage	800 mg/kg + 800 mg/kg	9 days	$7.2x10^{10}$ "	chrysotile crocidolite	24 hours	stomach, heart, pancreas, blood, kidney, lung, liver, spleen	-	EM	+	sign. elevated chrysotile and crocidolite in heart and blood, chrysotile in stomach and pancreas	Kaczenski and Hallenbeck, 1984
Man In drinking water	"high amphiboles", fiber length 1.5 um, diameter <0.2 um); control population "low amphiboles"	up to 14 years	-	amphibole	-	lungs, jejunum, liver	$8x10^{-3}$	EM	lung amphibole content***: $0.5x10^{5}$ fibers/gram jejunum amphibole content***: 0 fibers/gram liver amphibole content***: $0.4x10^{5}$ fibers/gram	$16.2x10^{5}$ fibers/gram $0.3x10^{5}$ fibers/gram $5.9x10^{5}$ fibers/gram	Carter and Taylor, 1980

Table 2. (continued)

Route of administration	Calculated daily dose (mg/kg b.w.)	Duration	Cumulative calculated fiber dose (f/g b.w.)	Type of fiber	Recovery period	Tissues examined	Calculated recovery rate	Analysis	Results(EM) Control	Test	Author(s)
In drinking water	$2x10^8$ fibers/l; control population	1.5-24 yr	$6.7x10^3$	chrysotile	-	urine	0.13	EM	$0.83x10^6$ chrysotile fibers/l	$0.92x10^6$ chrysotile fibers/l	Boatman et al., 1983
	$2x10^6$ fibers/l	3-19 yr	67								
In drinking water	"high amphiboles"; control population filtered water	?	-	amphibole	-	urine	-	EM	$2.3x10^4$ fibers/l	$6.6x10^5$ fibers/l	Cook and Ohlson, 1979
Oral medicine	150 mg/kg of average fiber length 0.8 um	6 months	$2.7x10^{11}$	attapulgite	?	urine	$1x10^{-6}$	?	-	$3x10^5$ fibers/ml	Bignon et al., 1980

*) animals were offspring from asbestos-fed mothers

**) Recovered fibers per g tissue or g b.w. / ingested fibers per g b.w.

***) test samples probably contaminated with amphiboles (Cook, 1983)

Table 3. Animal ingestion studies, carcinogenic effects.

Species	Number of animals (m=male, f=female)	Regimen	Calculated approximate daily dose (mg/kg b.w.)	Fiber type	Effects	Author(s)
Rat (SD)	20	300 mg/day in cottage cheese, lifetime	750	amosite	No increased tumor incidence	Hilding et al., 1981
	20	control	-			
Rat (F344)	100 m, 100 f	10% in diet up to 32 months	500	chrysotile B	No increased tumor incidence, 3/189 adenocarcinoma of colon, 1/189 adenoma of colon, 1/189 mesothelioma in abdomen.	Donham et al., 1980
	100 m, 100 f	10% in diet (positive control)	-	nonnutritive cellulose	No increased tumor incidence, 2/197 adenocarcinomas of colon.	
	100 m, 100 f	control	-	-	3/115 adenocarcinomas of colon.	
Rat (F344)	250 m, 250 f	1% in diet, lifetime	500	shortrange chrysotile	No increased tumor incidence, m 4%, f 5% tumors of alimentary tract.	NTP, 1985
	250 m, 250 f	1% in diet, lifetime	500	intermediate range chrysotile	No increased malignant tumor incidence, increased benign epithelial neoplasms in descending colon of males, m 8%, f 3% tumors of alimentary tract.	
	100 m, 100 f	1% in diet, lifetime + preweaning gavage of similar dose	500	intermediate range chrysotile	No increased tumor incidence, m 7%, f 5% tumors of alimentary tract.	
	88 m,	control		-	M 2%, f 3% tumors of alimentary	

Table 3. (continued)

Species	Number of animals (m=male, f=female)	Regimen	Calculated approximate daily dose (mg/kg b.w.)	Fiber type	Effects	Author(s)
	88 f				tract.	
Rat (F344)	250 m, 250 f	1% in diet, lifetime	500	amosite	Increased C-cell adenomas of thyroid in males (m 20%, f 12%), increased mononuclear leukemia in males (m 42%, f 33%).	McConnell et al., 1983b
	100 m, 100 f	1% in diet, lifetime + preweaning gavage of a similar dose	500	amosite	Increased mononuclear leukemia in males (m 49%, f 34%).	
	118 m, 118 f	control	-	-	Incidence C-cell carcinoma of thyroid m 14%, f 14%, incidence mononuclear leukemia m 32%, f 33%.	
Rat (F344)	250 m, 250 f	1% in diet, lifetime	500	tremolite	No increased tumor incidence	McConnell et al., 1983b
	118 m, 118 f	control	-	-	-	
Rat (Wistar)	40 m	1% in diet, up to 30 months (in 5% corn oil)	500	chrysotile	No increased tumor incidence	Cunningham et al., 1977
	40 m	control	-	-	-	
Rat (Wistar)	22 m	250 mg/week in margarine, 25 months	90	chrysotile A	No increased malignant tumor incidence, increased incidence of benign neoplasms (11/22),	Bolton et al., 1982

Table 3. (continued)

Species	Number of animals (m=male, f=female)	Regimen	Calculated approximate daily dose (mg/kg b.w.)	Fiber type	Effects	Author(s)
					mainly of mesenteric hemangiomas (4/22).	
	24 m	250 mg/week in margarine, 25 months	90	amosite	No increased tumor incidence, 1/24 gastric leiomyosarcoma.	
	22 m	250 mg/week in margarine, 25 months	90	crocidolite	No increased tumor incidence.	
	24 m	margarine-fed control	-	-	No increased tumor incidence.	
	23 m	control	-	-	-	
Rat (SD)	30	20 mg/day, 7 months + 20 mg/day, rest lifespan, in cottage cheese	50	chrysotile amosite	No increased tumor incidence	Hilding et al., 1981
	20	control	-	-		
Rat (SD)	24 m, 16 f	1.5% in diet, cumulative dose 1900 mg in 63 weeks, up to 75 weeks of age	10	crocidolite	No increased tumor incidence in intestinal wall.	Bonser and Clayson, 1967
Rat (Wistar)	16 m, 16 f	100 mg/day; 101 days in 5 months;	250	talc	No increased tumor incidence, 1 leiomyosarcoma of the	Wagner et al., 1977

Table 3. (continued)

Species	Number of animals (m=male, f=female)	Regimen	Calculated approximate daily dose (mg/kg b.w.)	Fiber type	Effects	Author(s)
		lifetime follow-up			stomach.	
	16 m, 16 f	100 mg/day; 101 days in 5 months; lifetime follow-up	250	chrysotile (SFA, super fine with known carcinogenic potency)	No increased tumor incidence, 1(0?) leiomyosarcoma of stomach.	
	8 m, 8 f	control	-	-	-	
Rat (Wistar)	31	10 mg/week in butter for 16 weeks; lifetime follow-up	3.6	chrysotile	No increased tumor incidence.	Gross et al., 1974
	33	5 mg/week in butter for 16 weeks; lifetime follow-up	1.8	crocidolite	No tumors.	
	35	10 mg/week in butter for 16 weeks; lifetime follow-up	3.6	crocidolite	No increased tumor incidence.	
	24	butterfed control	-	-	No tumors.	
Rat (Wistar)	35 + 28	10 mg/week in butter for 18 weeks; lifetime	3.6	crocidolite (2 varieties)	No tumors.	Gross et al., 1974

Table 3. (continued)

Species	Number of animals (m=male, f=female)	Regimen	Calculated approximate daily dose (mg/kg b.w.)	Fiber type	Effects	Author(s)
	24	follow-up control	-	-	No tumors.	
Hamster (Syrian golden)	250 m, 250 f	1% in diet, lifetime	1200	shortrange chrysotile	Increased incidence of primary tumors in males, caused by increase of adrenal cortical adenomas (11%).	McConnell et al., 1983a
	250 m, 250 f	1% in diet, lifetime	1200	intermediate range chrysotile	Increased incidence of primary tumors in males, caused by increase of adrenal cortical adenomas (10%).	
	250 m, 250 f	1% in diet, lifetime	1200	amosite	No increased tumor incidence	
	3x126 m, 3x126 f	control	-	-	Primary tumor incidence m 20%; incidence adrenal cortical adenomas m 3-7%.	
Hamster (Syrian golden)	60	50 mg/l drinking water, up to 23 months	34	amosite	No increased tumor incidence.	Smith et al., 1980 (cited in Toft et al., 1984)
	60	5 mg/l drinking water, up to 23 months	3.4	amosite	No increased tumor incidence, 1 peritoneal mesothelioma.	
	60	0.5 mg/l drinking water, up to 23 months	0.34	amosite	No increased tumor incidence.	
	120	control	-	-	-	

Table 4. Asbestos mass concentration in air related to carcinogenic effects in rats after longterm inhalation.

Species	Number of animals	Asbestos type	Concentration	Duration exposure*	Duration experiment	Effects			Author(s)
						Lung tumors	Mesotheliomas	Total	
Rat	61	chrysotile	86 mg/m3	62 weeks	16-21 months	9/42	1/42	24%	Gross et al., 1967
	40	control	-		-	3/19		16%	
Rat	69	chrysotile	50 mg/m3	2 years**	?	3/43		7%	Reeves et al., 1974
	69	crocidolite	50 mg/m3	2 years**	?	4/46		9%	
	69	amosite	50 mg/m3	2 years**	?	2/46	1/46	7%	
	10-12	control	-					0%	
Rat (Wistar)	24	Canadian chrysotile	10-11 mg/m3	24 months	24 months	5/21	1/21	29%	Wagner et al., 1974
	20	Zimbabwean chrysotile	10-11 mg/m3	24 months	24 months	10/17		59%	
	20	crocidolite	10-11 mg/m3	24 months	24 months	4/18		22%	
	21	amosite	10-11 mg/m3	24 months	24 months	9/21		43%	
	19	anthophyllite	10-11 mg/m3	24 months	24 months	9/18	1/18	56%	
	48	control	-					0%	
Rat (Wistar)	23	Canadian chrysotile	10-11 mg/m3	12 months	24 months	7/23	3/23	43%	Wagner et al., 1974
	27	Zimbabwean chrysotile	10-11 mg/m3	12 months	24 months	13/27		48%	
	26	crocidolite	10-11 mg/m3	12 months	24 months	9/26	2/26	42%	
	25	amosite	10-11 mg/m3	12 months	24 months	1/25		4%	
	28	anthophyllite	10-11 mg/m3	12 months	24 months	5/28	1/28	21%	
	48	control	-					0%	

Table 4. (continued)

Species	Number of animals	Asbestos type	Concentration	Duration exposure*	Duration experiment	Effects Lung tumors	Effects Mesotheliomas	Effects Total	Author(s)
Rat	48	chrysotile	10 mg/m3	1 year	860 days	8/40		20%	Davis et al., 1978
(Wistar)	48	crocidolite	10 mg/m3	1 year	860 days	0/40		0%	
	48	amosite	10 mg/m3	1 year	860 days	0/43		0%	
	20	control	-					0%	
Rat	48	amosite	10 mg/m3	1 year	29 months	0/40		0%	Davis et al., 1980
(Wistar)	48	control	-					0%	
Rat	48	crocidolite	5 mg/m3	1 year	860 days	0/43	1/43	2%	Davis et al., 1978
(Wistar)	48	chrysotile	2 mg/m3	1 year	860 days	2/42	1/42***	7%	
	48	control	-					0%	
Rat	48	chrysotile	2 mg/m3	1 year	29 months	2/40	1/40	8%	Davis et al., 1980
(Wistar)	48	control	-					0%	
Rat	80	chrysotile	1 mg/m3	18 months	24 months	0/38		0%	Platek et al., 1985
(SD)	80	control	-			0/45		0%	

*) 30-35 hours/week unless otherwise stated

**) 16 hours/week

***) peritoneal mesothelioma; all others pleural mesotheliomas

Table 5. Asbestos fiber concentration in air and fiber size related to carcinogenic effects in rats after longterm inhalation.

Number of animals	Asbestos type	Concentration* (fibers >5um/l)	(mg/m3)	Fiber size characteristics %>5um length	%>20um length	Effects Lung tumors	Mesotheliomas	Total	Author(s)
48	chrysotile	2.0×10^6	10	35%	5%	8/40		20%	Davis et al., 1978
48	crocidolite	8.6×10^5	10	15%	0.5%	0/40		0%	
48	amosite	5.5×10^5	10	18%	0.3%	0/43		0%	
48	crocidolite	4.3×10^5	5	15%	0.5%	0/43	1/43	2%	
48	chrysotile	3.9×10^5	2	35%	5%	2/42	1/42	7%	
69	crocidolite	1.1×10^6 **	50	-	-	4/46		9%	Reeves et al., 1974
69	amosite	8.6×10^5 **	50	-	-	2/46	1/46	7%	
69	chrysotile	5.4×10^4 **	50	-	-	3/43		7%	
48	amosite	-	10	30%	11%	-	-	>30%	Davis (IPCS, 1986)
48	amosite	-	10	1%	-	-	-	0%	
24	UICC chrysotile	3.2×10^6	11	-	-	-	-	UICC gave more lung tumors than Grade 7 (SFA?)	Wagner (IPCS, 1986)
24	Grade 7 chrysotile	1.0×10^6	11	-	-	-	-		
24	SFA chrysotile	4.3×10^5	11	"superfine"		-	-		
80	chrysotile	8.0×10^2 ***	1	<1%	-	0/38	0/38	0%	Platek et al., 1985

- = not reported

*) 30-35 hours/week, 1 year unless otherwise stated

**) 16 hours/week, 2 years

***) counted by light microscope; electron microscopic counting: 3×10^3 f/l

Table 6. Carcinogenic effects of asbestos inhalation in rats in relation to the duration of exposure (from: Wagner et al., 1974).

Number of animals	Asbestos type	Concentration	Duration of exposure (7 hrs/day; 5 days/week)	Duration of experiment	Effects		
					Lung tumors	Mesotheliomas	Total
49	Canadian chrysotile	10 mg/m3	1 day	24 months	1/42		2%
49	Zimbabwean chrysotile	15			1/45		2%
49	crocidolite	13			1/43	1/43	5%
49	amosite	14			0/45	1/45	2%
49	anthophyllite	13			0/44		0%
48	control	-			0/44		0%
52	Canadian chrysotile	12 mg/m3	3 months	24 months	3/34		9%
52	Zimbabwean chrysotile	12			3/39		8%
52	crocidolite	13			2/36	1/36	8%
52	amosite	12			0/37		0%
52	anthophyllite	14			0/37		0%
58	control	-			0/40		0%
24	Canadian chrysotile	10 mg/m3	6 months	24 months	1/17		6%
25	Zimbabwean chrysotile	11			3/19		16%
24	crocidolite	11			0/18		0%
24	amosite	11			1/18		6%
24	anthophyllite	11			2/18		11%
48*	control	-			0/42		0%

Table 6. (continued)

Number of animals	Asbestos type	Concentration	Duration of exposure (7 hrs/day; 5 days/week)	Duration of expriment	Effects		
					Lung tumors	Mesotheliomas	Total
23	Canadian chrysotile	11 mg/m3	12 months	24 months	7/23	3/23	43%
27	Zimbabwean chrysotile	11			13/27		48%
26	crocidolite	11			9/26	2/26	42%
25	amosite	11			1/25		4%
28	anthophyllite	11			5/28	1/28	21%
48*	control	-			0/42		0%
24	Canadian chrysotile	10 mg/m3	24 months	24 months	5/21	1/21	29%
20	Zimbabwean chrysotile	10			10/17		59%
20	crocidolite	10			4/18		22%
21	amosite	11			9/21		43%
19	anthophyllite	11			9/18	1/18	56%
48*	control	-			0/42		0%

Table 7. Differences in exposure regimen (intermittent peak doses versus regular even doses) related to carcinogenic effects in rats after longterm inhalation of asbestos (from: Davis et al., 1978).

Number of animals	Asbestos type	Concentration (mg/m3)*	Hours/week exposure (1 year)	Duration experiment	Effects		
					Lung tumors	Mesotheliomas	Total
48	chrysotile	10 mg/m3	7(1 day)	29 months	2/43		5%
48	chrysotile	2 mg/m3	35(5 days)	29 months	2/40	1/40	8%
48	amosite	50 mg/m3	7(1 day)	29 months	2/44		5%
48	amosite	10 mg/m3	35(5 days)	29 momths	0/40		0%

*) the cumulative fiber dose was approximately the same for all 4 groups

Table 8. Fibrogenicity of asbestos in animals after inhalation for various periods of time.

Species	Asbestos type	Concentration and fiber size				Duration of exposure	Effects (at time of measurement from first exposure)	Author(s)
		mg/m3	f>5um/l	%>5um	%>20um			
		(6-8 hrs/day, 5 days/week unless otherwise stated)						
Rat	crocidolite	50(16hrs/w)	1.1×10^6	-	-	2 years	Highest degree of asbestosis for crocidolite	Reeves et al., 1974
	amosite	50(16hrs/w)	8.6×10^5	-	-	2 years		
	chrysotile	50(16hrs/w)	5.4×10^4	-	-	2 years		
Rat	SFA chrysotile	11	-	"very fine"		1 year	Sligth to moderate fibosis after 1 year with progression after termination of exposure	Wagner et al., 1977
	Italian talc	11	-	-	-	1 year	Very similar fibrosis with progression	
Rat	amosite, anthophyllite, crocidolite, chrysotile (Canadian), chrysotile (Zimbabwean)	10-15	-	-	-	1 day, 8 weeks, 3, 6, 12 and 24 months	Gradually increasing degree of fibrosis with time; amosite slightly less than other varieties; progression with time after termination of exposure (see fig. 1)	Wagner et al., 1974
Rat							At 12 , 18 and 29 months:	Davis et al., 1978
	chrysotile	10	2.0×10^6	35%	5%	1 year	19.3, 17.1 and 15.0% peribronchiolar fibrosis**	
	crocidolite	10	8.6×10^5	15%	0.5%	1 year	2.7, 4.3 and 3.9%	
	amosite	10	5.5×10^5	18%	0.3%	1 year	4.1, 5.1 and 4.2%	
	crocidolite	5	4.3×10^5	15%	0.5%	1 year	2.8, 2.3 and 2.5%	
	chrysotile	2	3.9×10^5	35%	5%	1 year	10.7, 9.9 and 7.5%	
Rat							At 12 , 18 and 29 months:	Davis et al., 1978
	chrysotile	10	2.0×10^6	35%	5%	1 year	0.5, 0.9 and 9.2% interstitial fibrosis**	
	crocidolite	10	8.6×10^5	15%	0.5%	1 year	0 , 0.1 and 1.4%	

Table 8. (continued)

Species	Asbestos type	Concentration and fiber size				Duration of exposure	Effects (at time of measurement from first exposure)	Author(s)
		mg/m3	f>5um/l	%>5um	%>20um			
		(6-8 hrs/day, 5 days/week unless otherwise stated)						
	amosite	10	$5.5x10^5$	18%	0.3%	1 year	0.9, 0.1 and 2.6%	
	crocidolite	5	$4.3x10^5$	15%	0.5%	1 year	0.4, 0 and 0.8%	
	chrysotile	2	$3.9x10^5$	35%	5%	1 year	0.4, 0.8 and 3.9%	
Rat							At 12 , 18 and 29 months:	Davis et al., 1980
	amosite	50(1d/w)	-	18%	0.3%	1 year	6.2, 5.4 and 2.9% peribronchiolar fibrosis**	
	amosite	10	$5.5x10^5$	18%	0.3%	1 year	4.1, 5.1 and 4.2%	
	chrysotile	10(1d/w)	-	35%	5%	1 year	6.8, 6.1 and 3.9%	
	chrysotile	2	$3.9x10^5$	35%	5%	1 year	10.7, 9.9 and 7.5%	
Rat							At 12, 18 and 29 months:	Davis et al., 1980
	amosite	50(1d/w)	-	18%	0.3%	1 year	0 , 1.2 and 5.8% interstitial fibrosis**	
	amosite	10	$5.5x10^5$	18%	0.3%	1 year	0.9, 0.1 and 2.6%	
	chrysotile	10(1d/w)	-	35%	5%	1 year	1.3, 1.1 and 6.8%	
	chrysotile	2	$3.9x10^5$	35%	5%	1 year	0.4, 0.8 and 3.9%	
Rat	amosite	10	-	30%	-	1 year	Extensive fibrosis	Davis, 1986
	amosite	10	-	1%	-	1 year	No fibrosis	
Rat	chrysotile	11	-	25%,10%>10um		3 months	Continuing process of interstitial fibrosis	Pinkerton et al., 1984
	chrysotile	11	-	25%,10%>10um		12 months	with increasing lung volume due to thickening of alveolar walls and air trapping	
Rat	chrysotile	1	$0.8\text{-}3x10^3$	<1%	-	18 months	No fibrosis	Platek et al., 1985
Rat	amosite	300	$3.1x10^6$	-	-	90 days	Marked collagenized fibrosis	Lee et al., 1981

Table 8. (continued)

Species	Asbestos type	Concentration and fiber size				Duration of exposure	Effects (at time of measurement from first exposure)	Author(s)
		mg/m3	f>5um/l	%>5um	%>20um			
		(6-8 hrs/day, 5 days/week unless otherwise stated)						
	Fybex*	80	2.9×10^6	-	-	90 days	Very slight collagenized fibrosis	
	PKT*	70	2×10^6	-	-	90 days	Very slight collagenized fibrosis	
	fiberglass	400	7×10^5	-	-	90 days	No fibrosis	
Rat	Fybex*	370	4.2×10^7	-	-	90 days	Moderate collagenized fibrosis	Lee et al., 1981
	Fybex*	80	1.4×10^7	-	-	90 days	Slight collagenized fibrosis	
	Fybex*	40	2.9×10^6	-	-	90 days	Very slight collagenized fibrosis	
Rat	chrysotile	11	-	-	-	91 days	First fibrosis at 8 months, no calcification	Ogisho et al., 1984
	crocidolite	11	-	-	-	91 days	Microcalcifications, fibrosis at 8 months	
Rat	chrysotile	-(3hrs/d)	5×10^6	26%	2%	30 days	Slight focal collagen formation from day 14 onwards, with progression in interstitium	Holt et al., 1964
	chrysotile	-(1.5hr/d)	5×10^6	26%	2%	45 days	Similar lesions, but smaller and less obvious	
Rat	chrysotile	15	-	-	3%	1 hour	Interstitial calcifications after 1 month with thickened alveolar duct bifurcations	Brody and Hill, 1982
Mouse	crocidolite	50(16hrs/w)	1.1×10^6	-	-	2 years	Mild to moderate fibrosis	Reeves et al., 1974
	amosite	50(16hrs/w)	8.6×10^5	-	-	2 years	Mild to moderate fibrosis	
	chrysotile	50(16hrs/w)	5.4×10^4	-	-	2 years	Very sligth fibrosis	
Mouse	chrysotile	11(2hrs/d)	-	-	-	75 days	Diffusely scattered focal fibrotic lesions	Bozelka et al., 1983b
Mouse	chrysotile	11	-	-	-	3 days	By 26 weeks minimal fibrosis in centrialveolar region of lungs	Boorman et al., 1984

Table 8. (continued)

Species	Asbestos type	Concentration and fiber size				Duration of exposure	Effects (at time of measurement from first exposure)	Author(s)
		mg/m3	f>5um/l	%>5um	%>20um			
		(6-8 hrs/day, 5 days/week unless otherwise stated)						
Guinea pig	crocidolite	50(16hrs/w)	$1.1x10^6$	-	-	2 years	Gradually developing fibrosis in all groups	Reeves et al., 1974
	amosite	50(16hrs/w)	$8.6x10^5$	-	-	2 years		
	chrysotile	50(16hrs/w)	$5.4x10^4$	-	-	2 years		
Guinea pig	amosite	300	$3.1x10^6$	-	-	90 days	Marked collagenized fibrosis	Lee et al., 1981
	Fybex*	80	$2.9x10^6$	-	-	90 days	Very slight collagenized fibrosis	
	PKT*	70	$2 x10^6$	-	-	90 days	No fibrosis	
	fiberglass	400	$7 x10^5$	-	-	90 days	No fibrosis	
Guinea pig	Fybex*	370	$4.2x10^7$	-	-	90 days	Moderate collagenized fibrosis	Lee et al., 1981
	Fybex*	80	$1.4x10^7$	-	-	90 days	Slight collagenized fibrosis	
	Fybex*	40	$2.9x10^6$	-	-	90 days	Very slight collagenized fibrosis	
Hamster	amosite+ chrysotile	1	$1.3x10^4$	-	-	15 months	Sligth pulmonary fibrosis only after 15 months, sligth increased emphysema after 6 months but not after 15 months	Wehner, 1986
	amosite+ chrysotile	10	$1.2x10^5$	-	-	15 months		
Hamster	amosite	300	$3.1x10^6$	-	-	90 days	Marked collagenized fibrosis	Lee et al., 1981
	Fybex*	80	$2.9x10^6$	-	-	90 days	Very slight collagenized fibrosis	
	PKT*	70	$2 x10^6$	-	-	90 days	Very slight collagenized fibrosis	
	fiberglass	400	$7 x10^5$	-	-	90 days	No fibrosis	
Hamster	Fybex*	370	$4.2x10^7$	-	-	90 days	Moderate collagenized fibrosis	Lee et al., 1981
	Fybex*	80	$1.4x10^7$	-	-	90 days	Slight collagenized fibrosis	
	Fybex*	40	$2.9x10^6$	-	-	90 days	Very slight collagenized fibrosis	

Table 8. (continued)

Species	Asbestos type	Concentration and fiber size				Duration of exposure	Effects (at time of measurement from first exposure)	Author(s)
		mg/m3	f>5um/l	%>5um	%>20um			
		(6-8 hrs/day, 5 days/week unless otherwise stated)						
Rabbit	crocidolite	50(16hrs/w)	$1.1x10^6$	-	-	2 years	Ligth to intermediate fibrosis in survivors	Reeves et al., 1974
	amosite	50(16hrs/w)	$8.6x10^5$	-	-	2 years	Ligth to intermediate fibrosis in survivors	
	chrysotile	50(16hrs/w)	$5.4x10^4$	-	-	2 years	Very sligth fibrosis in survivors	
Baboon	crocidolite	16	$1.1x10^6$	mean 1xd: 2x0.3um		lifetime	Slightly progressing fibrosis	Goldstein et al., 1983
	glass fiber	8	$1.1x10^6$	6x0.5um		lifetime	Similar lesions but less extensive	
Gerbil	crocidolite	50(16hrs/w)	$1.1x10^6$	-	-	2 years	Ligth to moderate fibrosis, focal	Reeves et al., 1974
	amosite	50(16hrs/w)	$8.6x10^5$	-	-	2 years	and generalized alveolar proteinosis	
	chrysotile	50(16hrs/w)	$5.4x10^4$	-	-	2 years	especially in amosite/crocidolite groups	

*)PTK = pigmentary potassium titanate; Fybex = potassium octatitanate

**) calculated % of lung tissue that was fibrotic

Table 9. Fibrogenic effects of asbestos in animals after intratracheal instillation

Species	Asbestos type	Administered dose(mg)	Regimen	Effects	Author(s)
Rat	UICC chrysotile	5 (20mg/kg b.w.)	single administration	Significant fibrotic reactions from day 7 onwards	Lemaire et al., 1985
	Very short 4T30 chrysotile	5 (20mg/kg b.w.)	single administration	Inflammation (alveolitis), no fibrosis	
Hamster	Chrysotile	5 (40mg/kg b.w.)	single administration	Progressing interstitial fibrosis with air flow obstruction and air trapping in secluded alveoli	Glassroth et al., 1984
Guinea pig	Amosite	30 (40mg/kg b.w.)	single administration	Asbestosis begins at any site in the parenchyma to which the fibers gain access; at 6 months similar response in both groups	Filipenko et al., 1985
		10 (13mg/kg b.w.)	single administration		
Guinea pig	Crocidolite short:<1% >5um length	25 (33mg/kg b.w.)	adminstered in 2-8 instillations	No fibrosis	Wright and Kuschner, 1977
	Crocidolite long:>80% >10um length	4 (5mg/kg b.w.)	" " "	Extensive interstitial fibrosis	
	Synthetic fluor amphibole short: <1% >5um lenght	12 (16mg/kg b.w.)	" " "	No fibrosis	
	Synthetic fluor amphibole long: 43%>5um, 16%>10um length	12 (16mg/kg b.w.)	" " "	Extensive interstitial fibrosis	
	Glass fiber short:7%<10um	25 (33mg/kg b.w.)	" " "	No fibrosis	

Table 9. (continued)

Species	Asbestos type	Administered dose(mg)	Regimen	Effects	Author(s)
	length Glass fiber long: 92%>10um length	12 (16mg/kg b.w.)	" " "	Minimal but definite fibrotic lesions	
	Very thin glass fiber short: 100%<5um length	25 (33mg/kg b.w.)	" " "	No fibrosis	
	Very thin glass fiber long: 50%>10um length	12 (16mg/kg b.w.)	" " "	Minimal but definite fibrotic lesions	
Guinea pig	Amosite	17.5 (23mg/kg b.w.)	single administration	Early effects (1-7 days) only alveolar, not interstitial: formation of small fibrin bundles within alveoli from 2 hours post-dosage onwards; regressing increased permeability of alveolar epithelium	Dodson et al., 1983, 1984
Sheep	Chrysotile	126 (3.2mg/kg b.w.)	1x/month during 6 months, 1x/week during next 6 months	Macrophage infiltrates into interstitium, with alveolitis, narrowed small airways and obstructed airflow	Begin et al., 1983
	Chrysotile	2 (0.05mg/kg b.w.)	" " "	No effects	

Table 10. Fibrous materials producing malignant neoplasms following intraperitoneal or intrapleural injection or implantation (Leineweber, 1980; Wagner et al., 1985; Pott, 1986).

Actinolite	Dawsonite
Aluminium oxide	Erionite
Aluminium silicate glass	Fibrous glass
Amosite	Mineral wool
Anthophyllite	Potassium titanite
Attapulgite	Silicone carbide
Borosilicate glass	Sodium aluminium carbonate
Chrysotile	Tremolite
Crocidolite	Wollastonite

Table 11. Correlation coefficients of logit of tumor probability with common logarithm of number of particles per microgram in different dimensional ranges (Stanton et al., 1981).

Fiber diameter, µm	Fiber length, µm		
	≤4	>4-8	>8
>4		-0.28	-0.30
>1.5-4	-0.45	-0.24	0.13
>0.25-1.5	0.01	0.45	0.68
≤0.25	0.20	0.63	0.80

Table 12. Some characteristics of epidemiological studies with asbestos in drinking water (Marsh, 1983; Erdreich, 1983; Toft et al., 1984).

Study area	Maximum duration of exposure (years)	Population size of studied area	Estimated exposure level ($\times 10^6$ f/l)	Type of fiber	Years of assessment of incidence(i)/ mortality(m)	Reference
Quebec	>50	30,000	1.1-1300	chrysotile	1964-1973(m)	Wigle, 1977
Canada	>50	110,000	0-1800	chrysotile	1966-1976(m)	Toft, 1981; Toft and Meek, 1983
California	>40	1,000,000*	0.016-36	chrysotile	1969-1971(i)	Kanarek et al., 1980
					1969-1975(i)	Conforti et al., 1981
Washington	>40	78,000*	0-556	chrysotile	1974-1977(i),	Polissar et al., 1982
		23,000*			1955-1975(m)	
Utah	20-30	24,000	n.r.	chrysotile	1967-1976(i)	Sadler et al., 1984
Florida	>25	46,000*	<1-10	chrysotile	1963-1976(m)	Millette et al., 1983
Connecticut	20	576,800	<0.1-0.7	chrysotile	1935-1973(i)	Harrington et al., 1978
					1955-1975(i)	Meigs et al. (cited by Meigs, 1983)
Minnesota	0-15	100,000	1-30	amphibole	1950-1969(m)	Mason et al., 1974 (cited by Marsh, 1983)
	15-20				1969-1971(i)	Levy et al., 1976
					1969-1974(i,m)	Sigurdson et al., 1981
	20-25		2-64		1969-1980(i)	Sigurdson, 1983

n.r. = not reported, probably low

*) high exposure subpopulation size

Table 13. Summary of studies of GI cancer risk in relation to ingested asbestos by site of neoplasm (adapted from Marsh, 1983; Erdreich, 1983).

Studied area	Site of neoplasm									All GI sites combined	Reference
	Esophagus	Stomach	Small intestine	Colon	Rectum	Biliary passage/ liver	Gall bladder	Pancreas	Peritoneum		
Quebec	00	M0	-	00	00	-	-	0F	-	00	Wigle, 1977
Canada	00	M0	-	00	00	-	-	00	-	M0	Toft, 1981; Toft and Meek, 1983
California	0F	MF	00	00	00	00	0F	0F	MF	MF	Kanarek et al., 1980
	MF	MF	00	M0	00	00	00	MF	0F	MF	Conforti et al., 1981
Washington	00	00	MF	00	00	00	00	00	00	-	Polissar et al., 1982
Utah	-	00	00	00	00	-	0F	00	00	-	Sadler et al., 1984
Florida	-	-	-	-	-	-	-	00	-	00	Millette et al., 1983
Connecticut	-	00	-	00	00	-	-	-	-	-	Harrington et al., 1978
	-	00	-	00	00	-	-	M0	-	-	Meigs et al. (cited by Meigs, 1983)
Minnesota	M0	MF	-	00	MF	00	-	0F	MF	MF	Mason et al., 1974 (cited by Marsh, 1983)
	00	M0	00	00	00	00	00	MF	00	00	Levy et al., 1976
	00	00	00	00	00	00	00	0F	00	00	Sigurdson et al., 1981

Positive association with ingested asbestos: M=present in males, F=present in females, 0=absent, -=not studied

Table 14. Summary of studies of non-GI cancer risk in relation to ingested asbestos by site of neoplasm (adapted from Marsh, 1983; Erdreich, 1983).

Studied area	Site of neoplasm									Reference
	Buccal cavity/ pharynx	Bronchus/ trachea/ lungs	Pleura	Prostate	Kidneys	Bladder	Brain/ CNS	Thyroid	Leukemia/ aleukemia	
Quebec	00	M0	-	0	00	00	00	-	00	Wigle, 1977
Canada	00	M0	-	0	00	00	00	-	00	Toft, 1981; Toft and Meek, 1983
California	-	M0	0F	0	0F	00	00	00	00	Kanarek et al., 1980
	-	00	0F	M	00	00	00	00	00	Conforti et al., 1981
Washington	00	00	-	M	00	00	M0	MF	M0	Polissar et al., 1982
Utah	-	-	-	-	M0	-	-	00	M0	Sadler et al., 1984
Florida	-	00	-	-	-	-	-	-	-	Millette et al., 1983
Connecticut	-	-	-	-	-	-	-	-	-	Harrington et al., 1978
	-	00	-	-	00	00	-	-	-	Meigs et al. (cited by Meigs, 1983)
Minnesota	-	M0	-	-	-	-	00	-	00	Mason et al., 1974 (cited by Marsh, 1983)
	-	-	-	-	-	-	-	-	-	Levy et al., 1976
	-	00	-	-	-	-	-	-	-	Sigurdson et al., 1981

Positive association with ingested asbestos: M=present in males, F=present in females, 0=absent, -=not studied

Table 15. Standardized mortality ratios (SMR) for cancers of the lung, GI tract and other sites, and number of deaths from mesothelioma and asbestosis in asbestos workers in various occupations. (Numbers of deaths in parentheses)

Type of exposure	Males Females	Cohort size	Years of follow-up	Years from onset exposure	SMR		Number of deaths			Other cancer significantly elevated	Reference
					Lung cancer	GI cancer	Mesothelioma pleural	Mesothelioma peritoneal	Asbestosis		
INSULATION WORKERS											
Mixed	M	632	1943-76	20+	7.10* (93)	2.91* (43)	11	27	41		Selikoff et al., 1979
	M	152	1945-65	15+	7.02* (10)	2.78* (5)	1	2	2		Kleinfeld et al., 1967
	M	170	1940-75	-	5.40* (27)	13.00* (13)	8	5 11**	19		Elmes and Simpson, 1977
	M	17800	1967-76	20+	4.16*(390)	1.67* (89)	63	112	168	Kidneys, larynx, pharynx, buccal cavity	Selikoff et al., 1979
GAS MASK MANUFACTURERS											
Crocidolite	MF	199	1939-75	-	8.75* (7)		3	6	4		McDonald and McDonald, 1978
	F	523	1951-77	10+	2.73* (10)	0.65 (7)	9	3	1	Ovary	Wignall and Fox, 1982
	F	757	1951-80	10+	1.97* (13)	1.25 (5)	3	2		Ovary	Acheson et al., 1982
	F	951	1941-78	-	1.90* (12)	0.49 (10)	13	4			Jones et al., 1980
Chrysotile	F	570	1951-80	10+	1.33 (6)	0.82 (4)	1	0			Acheson et al., 1982
MANUFACTURING											
Mixed	F	922	1936-75	10+	8.43* (27)	1.96* (20)	13	8	6.7		Newhouse and Berry, 1979
	MF	689	1959-71	20+	3.21* (27)	2.66* (13)	8	7	24		Nicholson , 1976
	M	1075	1941-73	Ret.	2.70* (63)	1.38* (55)	5	0	50		Henderson and Enterline, 1979
	M	4600	1936-75	10+	2.38*(103)	1.18 (40)	19	27	16.3		Newhouse and Berry, 1979
Amosite	M	820	1961-76	5+	3.08* (83)	1.23 (28)	7	7	30		Seidman et al., 1979
	M	4820	1947-78	-	1.96* (57)	1.11 (19)	4	1	8.9		Acheson et al., 1984
Chrysotile	M	254	1945-74	-	0.93 (4)	1.05 (4)	0	0			Weiss, 1977

Table 15. (continued)

Type of exposure	Males Females	Cohort size	Years of follow-up	Years from onset exposure	SMR		Number of deaths				Other cancer significantly elevated	Reference
					Lung cancer	GI cancer	Mesothelioma pleural	Mesothelioma peritoneal		Asbestosis		
TEXTILES												
Chrysotile	F	554	1940-75	-	8.24* (14)	1.33 (8)	1	1	2**	13.1		Robinson et al., 1979
	M	1261	1940-75	15+	3.36* (33)	1.24 (10)	0	1		17		Dement et al., 1983a,b
	MF	1493	1940-64	-	2.23* (33)	1.80* (16)	1	8		31		Mancuso and El-Attar, 1967
	M	822	1933-74	10+	2.14* (49)	1.02 (16)	9	0		20.6		Peto, 1977
	M	2543	1938-77	20+	2.00* (59)	1.52* (26)	0	1		20		McDonald et al., 1983a,b
	M	2722	1940-75	-	1.36* (49)	1.21 (50)	4	5	4**	59.5		Robinson et al., 1979
	M	4137	1938-77	20+	1.05 (53)	1.13 (54)	10	4		59		McDonald et al., 1983b
ASBESTOS CEMENT INDUSTRY												
Mixed	M	241	1963-80	15+	6.06* (20)	1.60 (4)	6	5		5.5		Finkelstein, 1983
	M	598	1957-80	10+	1.83* (12)	1.76* (19)	4	0		10.1		Albin et al., 1984
	M	5645	1940-74	20+	1.04 (51)	0.50 (25)	0	0				Weill, 1984
Chrysotile	M	1592	1936-77	15+	0.85 (22)	0.99 (14)	2	0		0		Thomas et al., 1982
MINING												
Chrysotile	M	544	1961-77	20+	2.25* (25)	1.05 (10)	1			26		Nicholson et al., 1979
	M	9767	1926-75	20+	1.25*(230)	1.03 (209)	10	0		46		McDonald et al., 1980
	M	952	1946-75	20+	1.03 (9)	1.03 (15)	1	0		21.1	Larynx	Rubino et al., 1979
	F	440	1926-75	20+	0.83 (1)		1	0		0		McDonald et al., 1980
Crocidolite	M	6200	1938-78	15+	1.57* (60)		17	0		14		Hobbs et al., 1980
Anthophyllite	MF	1092	1936-69	-	1.67* (21)	0.47 (7)	0	0		13		Meurman et al., 1974
Talc	M	260	1944-69	15+	2.89* (13)	1.01 (7)	0	1		29		Kleinfeld et al., 1974
(tremolite)	M	398	1947-75	-	2.70* (9)	1.00 (3)	0	0	1**	3.7		Brown et al., 1979
SHIPYARD ACTIVITIES												
Mixed	M	4264	1960-75	-	2.24*(123)	1.36 (66)				50.6	Kidney, urinary organs, larynx	Puntoni et al., 1979
	M	4779	1950-70	20+	1.73 (13)	-	0	0				Kolonel et al., 1980

Table 15. (continued)

Type of exposure	Males Females	Cohort size	Years of follow-up	Years from onset exposure	SMR		Number of deaths			Other cancer significantly elevated	Reference
					Lung cancer	GI cancer	Mesothelioma pleural	Mesothelioma peritoneal	Asbestosis		
	M	6292	1947-78	-	0.84 (84)	0.83 (63)		31**	9		Rossiter and Coles, 1980
FRICTION PRODUCTS MANUFACTURING											
Chrysotile	M	3177	1938-77	20+	1.49* (73)	1.14 (59)	0	0	0		McDonald et al., 1984
Mixed	M	7474	1942-80	10+	1.03 (143)	0.96(103)	8	0			Berry and Newhouse, 1983
	F	3708	1942-80	10+	0.53 (6)	1.06 (29)	2	0			Berry and Newhouse, 1983

*) significant at the 5% level

**) unspecified mesotheliomas

Table 16. Deaths among 17,800 asbestos insulation workers in the United States and Canada, January 1, 1967 - December 31, 1976, number of men 17,800, man-years of observation 166,853 (adapted from Selikoff et al., 1979).

Underlying cause of death	Number of deaths			Ratio observed/expected	
	Expected*	Observed			
		BE	DC	BE	DC
Total deaths, all causes	1658.9	2271	2271	1.37	1.37
Total cancer, all sites	319.7	995	922	3.11	2.88
Peritoneal mesothelioma	-	112	24	-	-
Pleural mesothelioma	-	63	25	-	-
Mesothelioma, n.o.s.	-	0	55	-	-
Cancer of lung	105.6	486	429	4.60	4.06
Cancer of kidney	8.1	19	18	2.36	2.23
Cancer of esophagus	7.1	18	18	2.53	2.53
Cancer of larynx	4.7	11	9	2.34	1.91
Cancer of pharynx/ buccal cavity	10.1	21	16	2.08	1.59
Cancer of skin	6.6	12	8	1.82	1.22
Cancer of colon/ rectum	38.1	59	58	1.55	1.52
Cancer of stomach	14.2	22	18	1.54	1.26
Cancer of prostate	20.4	30	28	1.47	1.37
Cancer of brain	10.4	14	17	1.35	1.63
Cancer of pancreas	17.5	23	49	1.32	2.81
Leukemia	13.1	15	15	1.15	1.15
Cancer of testes	1.9	2	1	1.05	0.52

Table 16. (continued)

Underlying cause of death	Number of deaths			Ratio observed/expected	
	Expected*	Observed			
		BE	DC	BE	DC
Cancer of bladder	9.1	9	7	0.99	0.77
Lymphoma	20.1	19	16	0.95	0.80
Cancer of liver/biliary passages	7.2	5	19	0.70	2.65
All other cancer	25.5	55	92	2.16	3.61
Noninfectious pulmonary diseases, total	59.0	212	188	3.59	3.19
Asbestosis	-	168	78	-	-
All other causes	1280.2	1064	1161	0.83	0.91

*) Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976

BE = Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical)

DC = Number of deaths as recorded from death certificate information only

\- = Rates and thus ratios are not available, but these have been rare causes of death in the general population

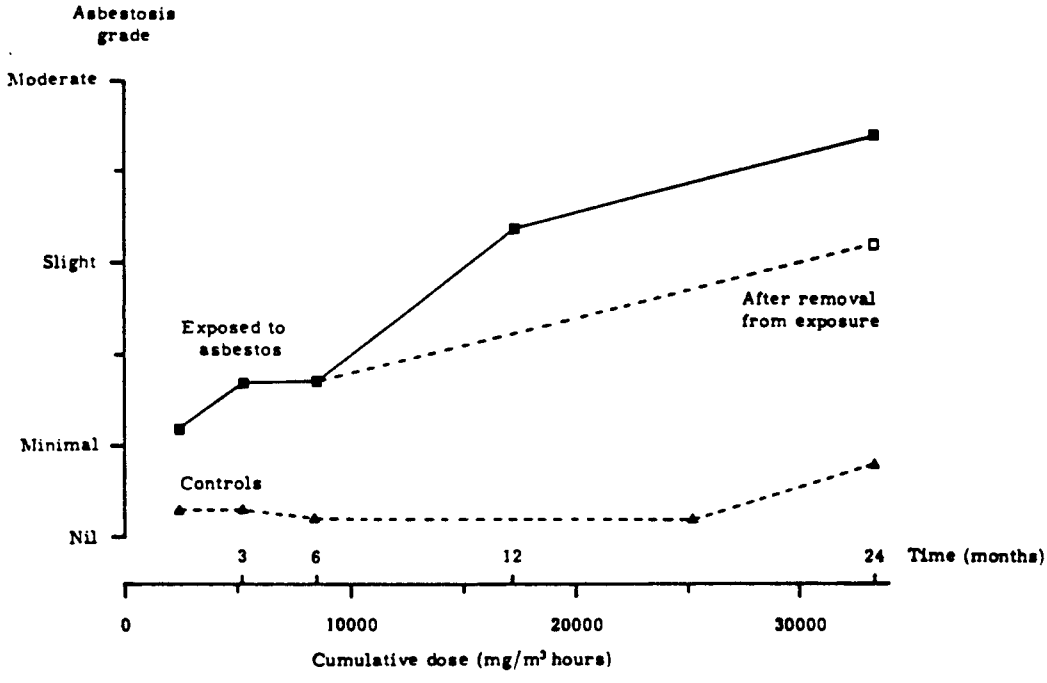

Fig. 1. Asbestosis in sacrificed rats in relation to dose and time (Wagner et al., 1974).

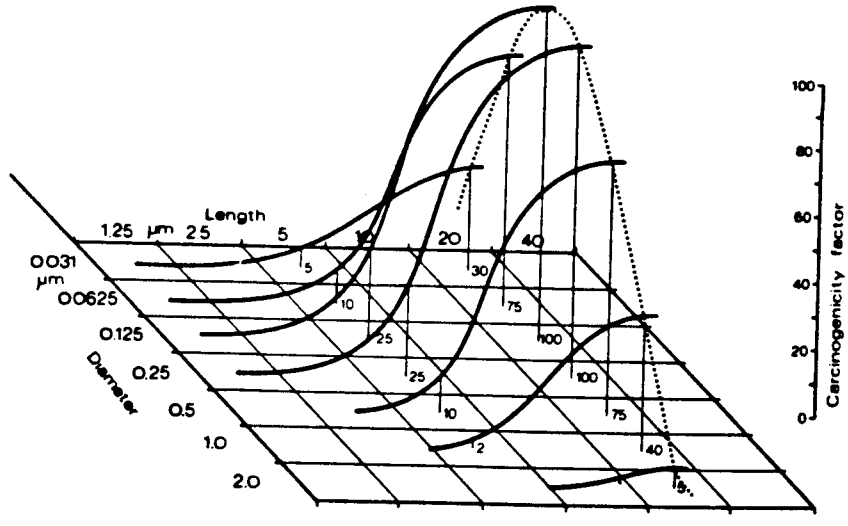

Fig. 2. Hypothesis on the carcinogenic potency of a fiber as a function of its size with some data on "carcinogenicity factors" (Pott, 1978).

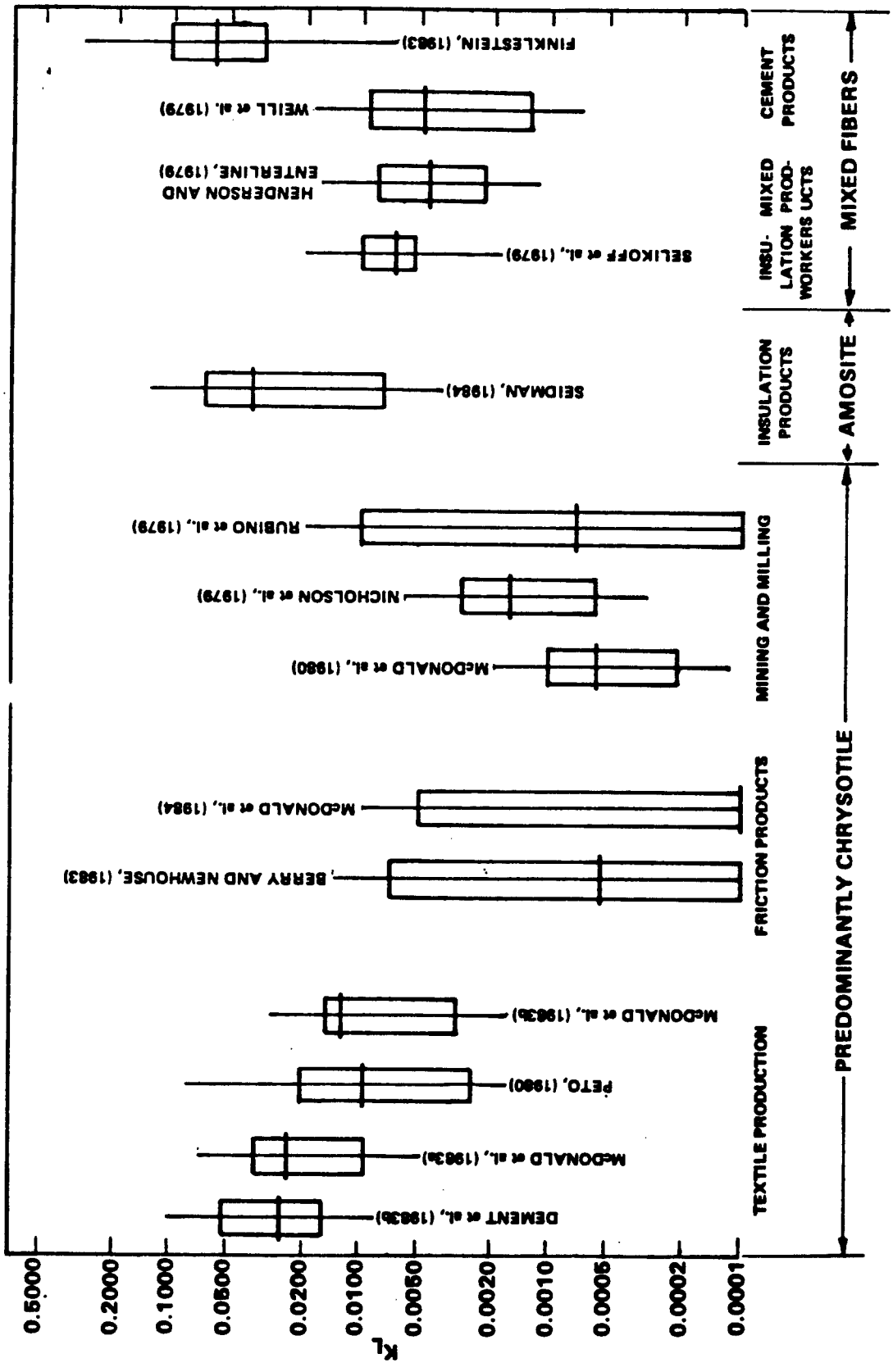

Figure 3 : Values of K_L, the fractional increase in lung cancer per f-y/ml of exposure in 14 asbestos exposed cohorts. The open bar reflects the estimated 95% confidence limits associated with measures of response. The line represents the uncertainties associated with measures of exposure, generally ± a factor of two.