



Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin

Hazards and risks from WHO fibres at the workplace

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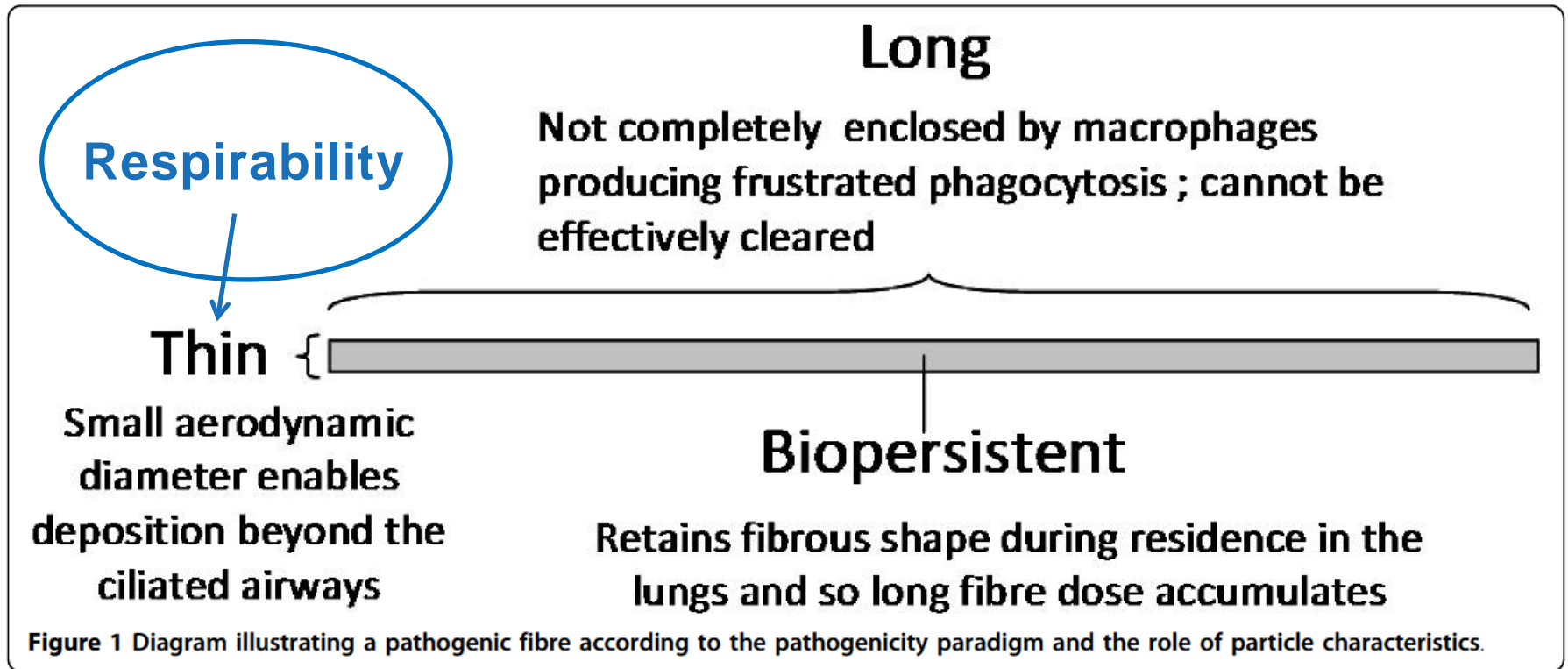
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Natural asbestos minerals: **highly potent** carcinogens

- appearing in several forms
- physical form (i.e. WHO fibre) determines effect
- induction of lung cancer and mesothelioma
- $10 \mu\text{g}/\text{m}^3$ (0.1 f/ml) equals 4/1000 cancer risk

Physical form determines carcinogenicity



Rigidity?

Why **respirable** dust?

upper airways: rapid elimination of dust via cilia

lung alveoli: **rather slow** elimination of dust by macrophages

Critical fibre dimension: the ,WHO' fibre convention

fibres are carcinogenic (lung and mesothelia) after inhalation if sufficiently

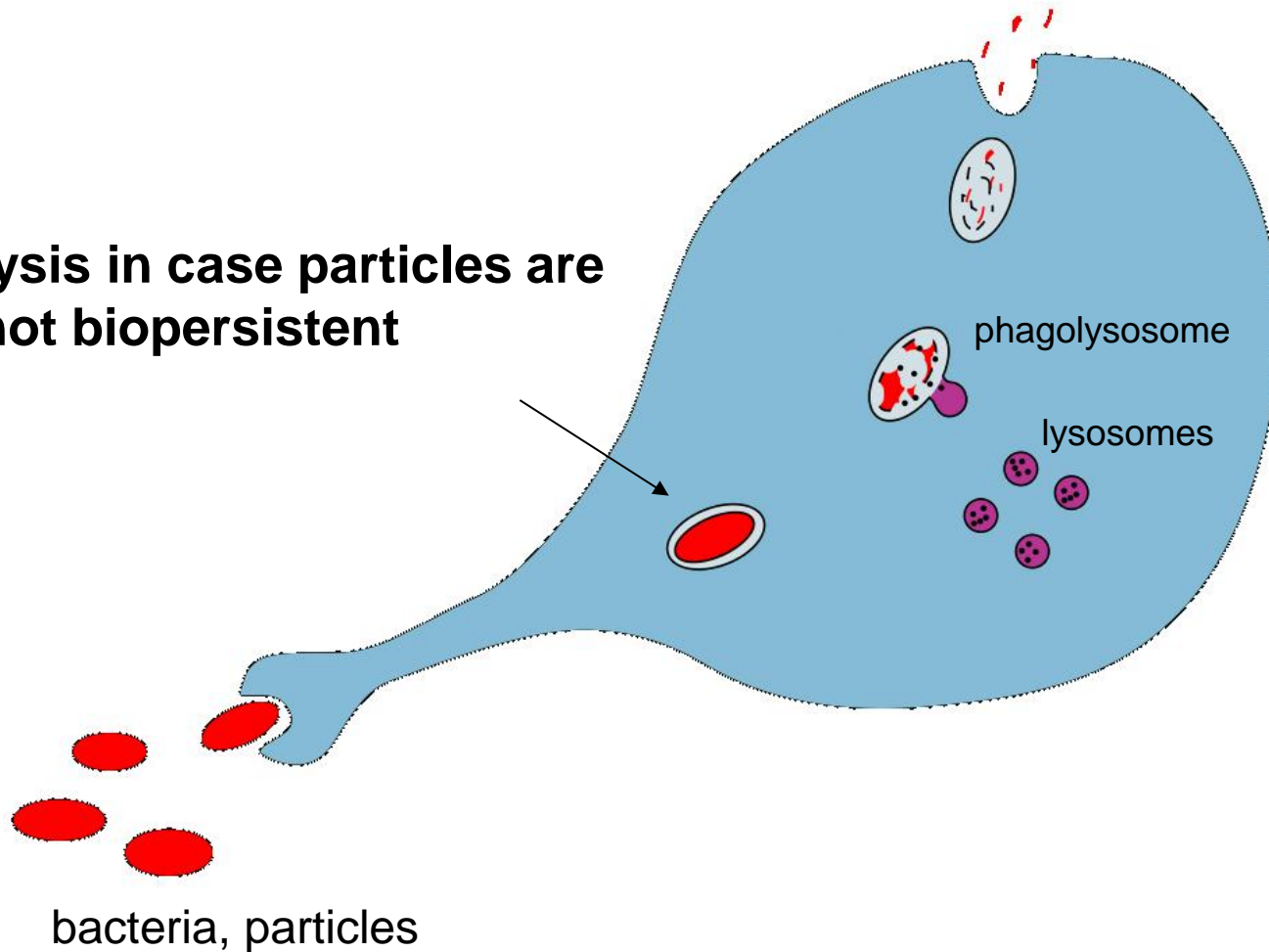
long - thin – biopersistent

length $> 5\ \mu\text{m}$
diameter $< 3\ \mu\text{m}$
aspect ratio $> 3:1$

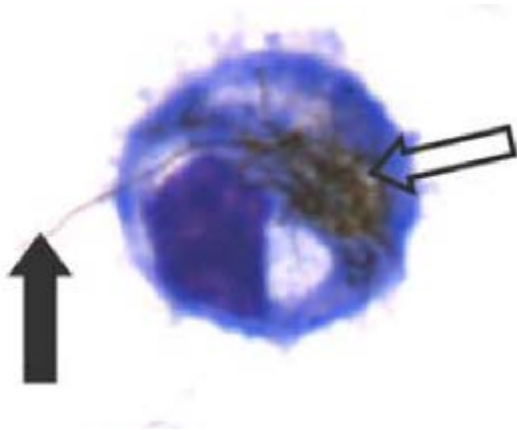
Alveolar macrophages and their job:

removal of bacteria and particles

lysis in case particles are
not biopersistent



Fibres: major mode of toxic action: frustrated phagocytosis



frustrated phagocytosis

**=> oxidative stress and
chronic inflammation**

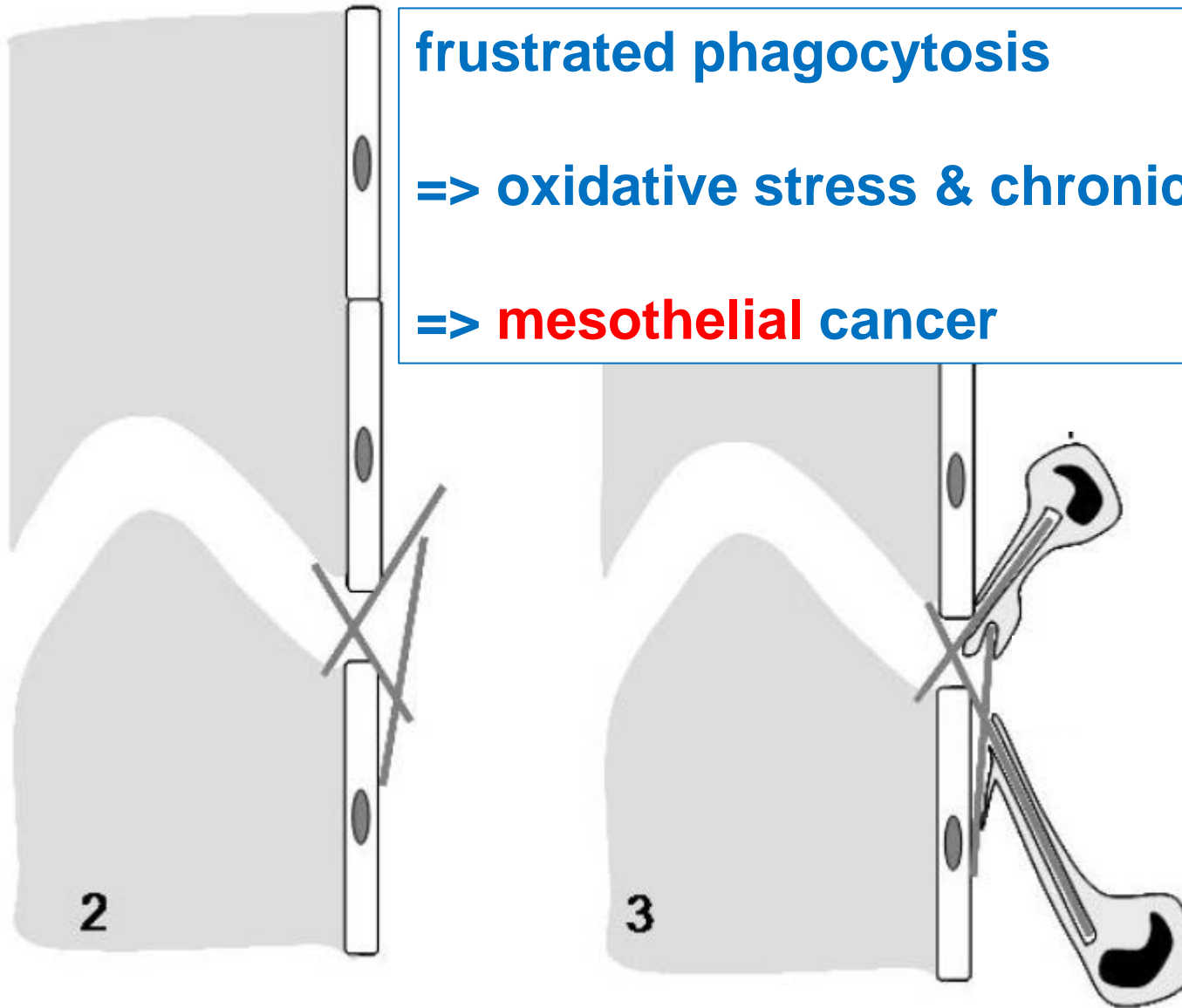
=> lung cancer

minimum fibre length ~ **15 μm** (Schinwald et al. 2012 Tox Sci 128:461)

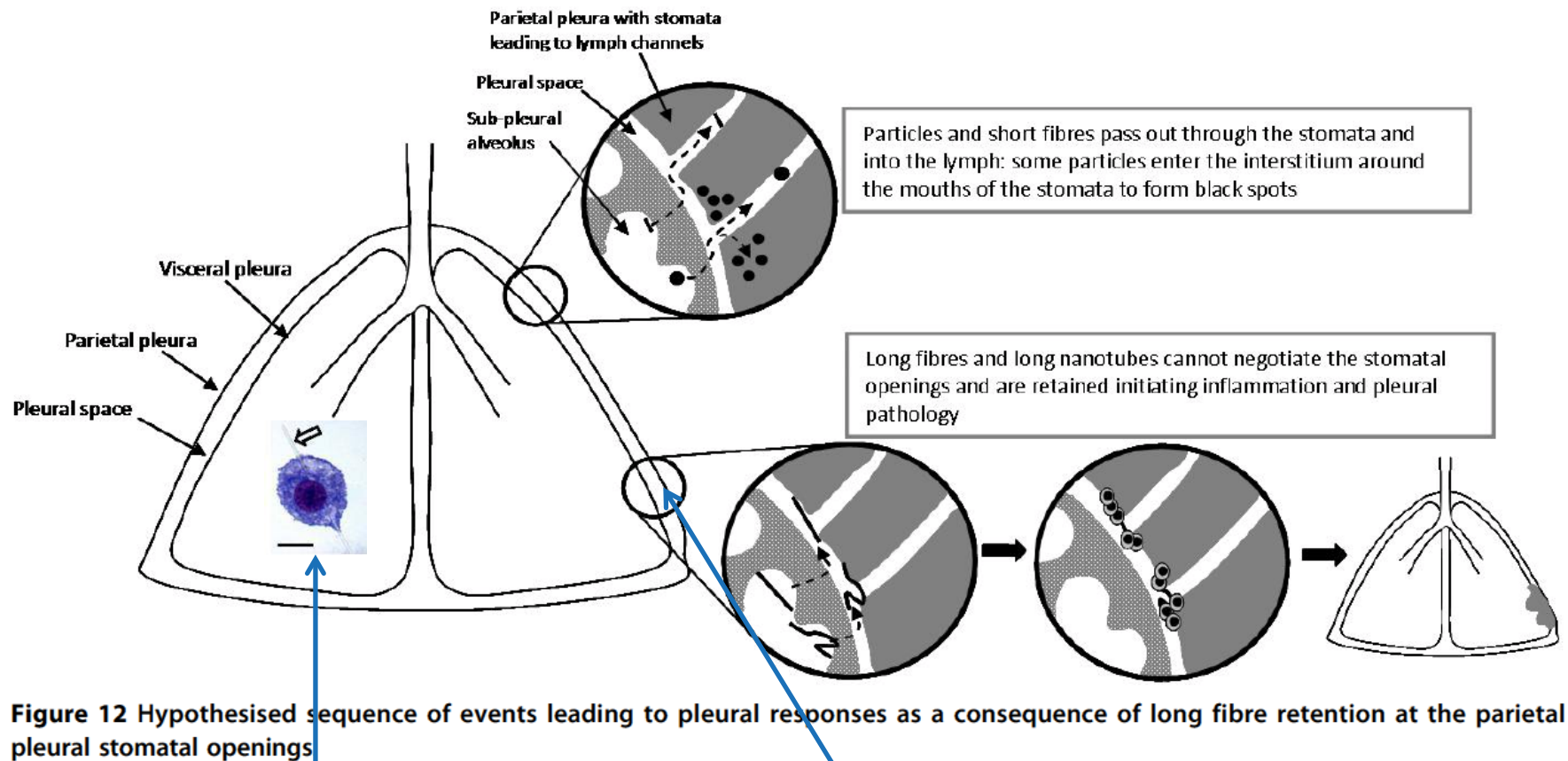
frustrated phagocytosis

=> oxidative stress & chronic inflammation

=> **mesothelial** cancer



minimum fibre length ~ **5 μm** (Schinwald et al. 2012 PFT 9:47)



lung cancer

mesothelial cancer

Fibres: additional hypotheses on mode of toxic action:

Evidence low so far

- direct piercing of mesothelial cells
- mechanical interaction with chromosomes

Data on fibre carcinogenicity

asbestos

carcinogenicity proven (lung and mesothelioma):

human epidemiology, animal testing

other WHO fibres (e.g. some man-made mineral fibres)

carcinogenicity proven (lung and mesothelioma):

animal testing

Carcinogenicity: fibre testing strategy

long-term inhalation

expensive

rat insensitive

intraperitoneal application, long-term experiment

simple and inexpensive

rat sensitive

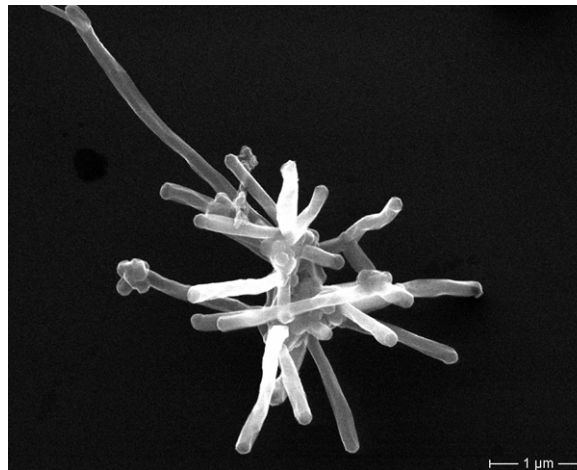
fibres in direct contact to mesothelial tissue

Comparison of the excess tumour risk of asbestos workers with the risk of rats after chronic inhalation

picture removed!

The risk of asbestos workers (dotted line) is derived by linear extrapolation of asbestos-induced death due to lung cancer or mesothelioma in asbestos workers (excluding mining and milling) after 25 years of exposure, when the fibre concentration increases from 1 to 5 fibres per mL air (Doll and Peto, 1985; HEI-AR, 1991). The regression line for the chronic rat inhalation studies is calculated from test results of different authors and different asbestos samples.

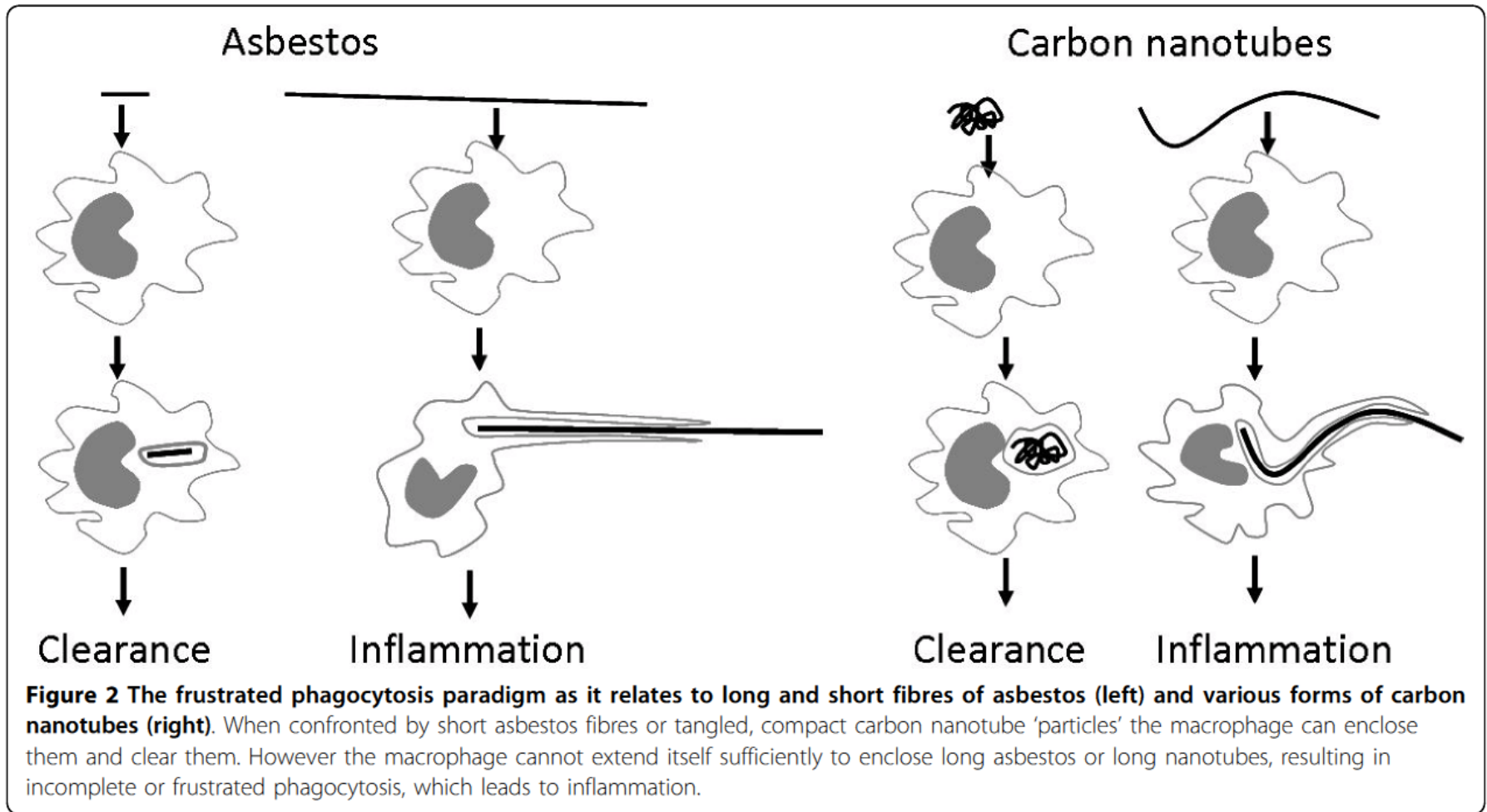
Which other fibrous material is acting like asbestos?



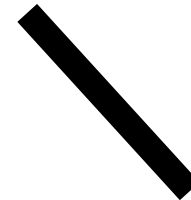
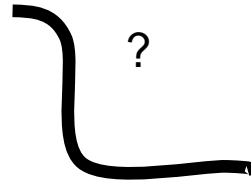
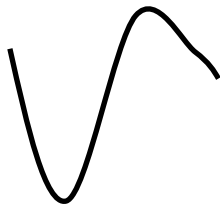
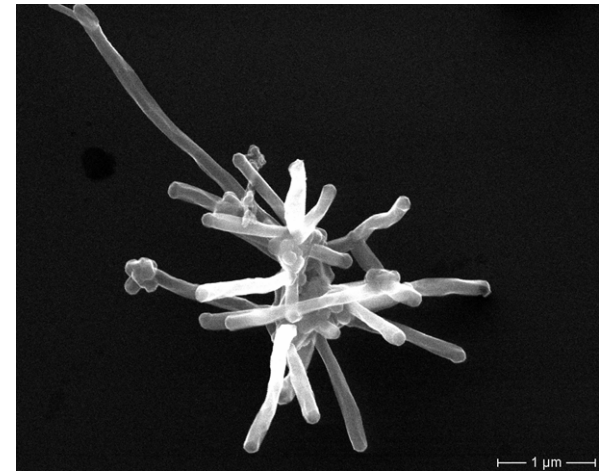
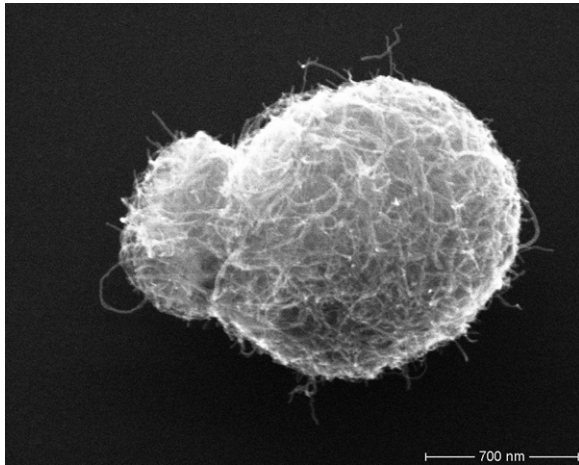
rigid carbon
nanotubes

in case rigid biodurable fibre of WHO dimension

Additional criterion: rigidity



Fibrous material: acting like asbestos?



tangled: acts like granular particle
low(er) carcinogenic potency

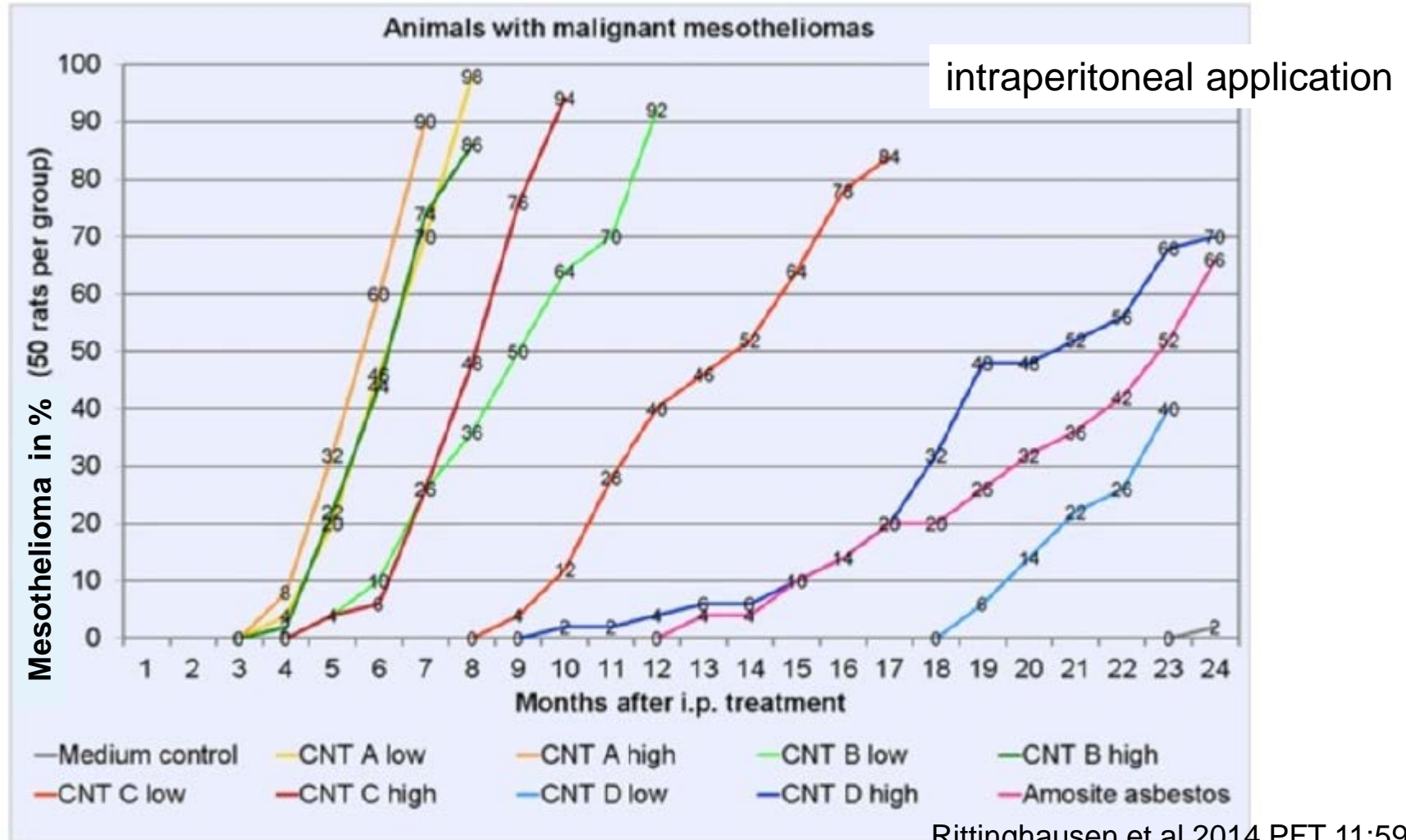
rigid: acts like asbestos
high carcinogenic potency

hypothesis ,rigid': diameter > 25-35 nm

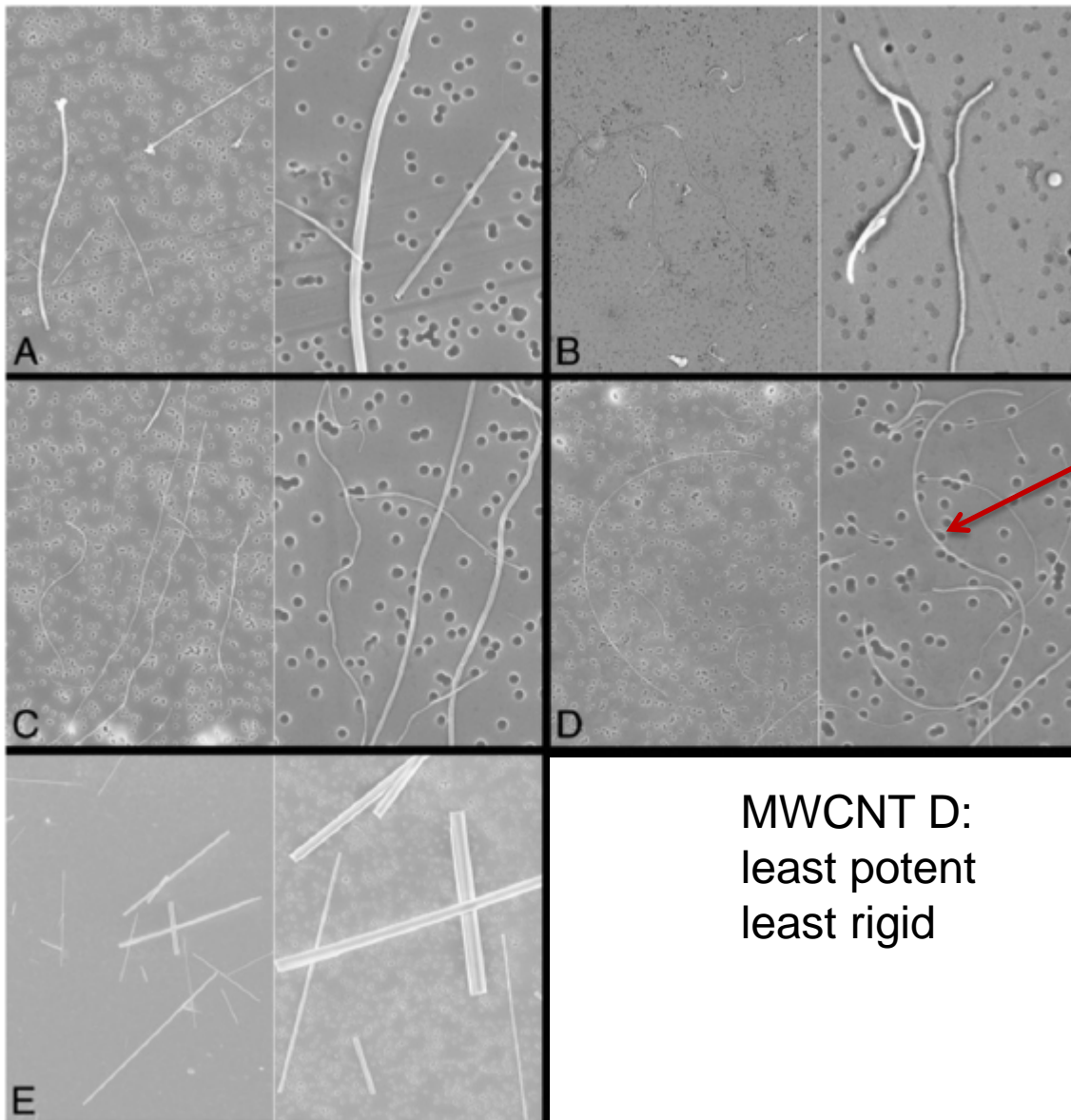
pics BAuA

**What do we know on
MWCNT carcinogenicity
so far?**

Rigid MWCNT more potent carcinogens than expected



Rittinghausen et al 2014 PFT 11:59



Amosite

MWCNT D:
least potent
least rigid

magnification
MWCNT 10000, 30000
Amosite 2000, 7000

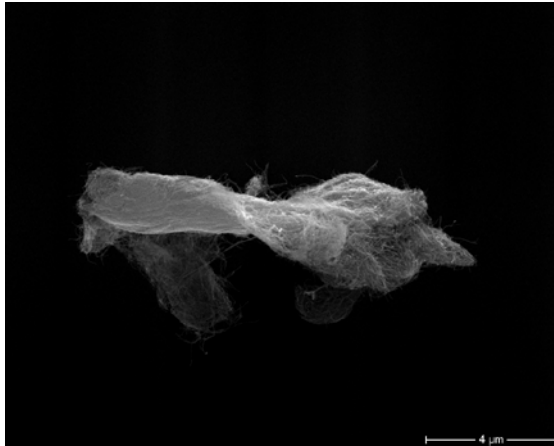
MWCNT: rat lung carcinogen also after inhalation

mg/m ³	0	0.02	0.2	2
adenoma	1	1	7	5
carcinoma	1	1	8	11

2-yr study, whole-body inhalation, aerosolized dry MWCNT

Fukushima et al. unpublished

Fibrous MWCNT: **rigid** ones acting like asbestos

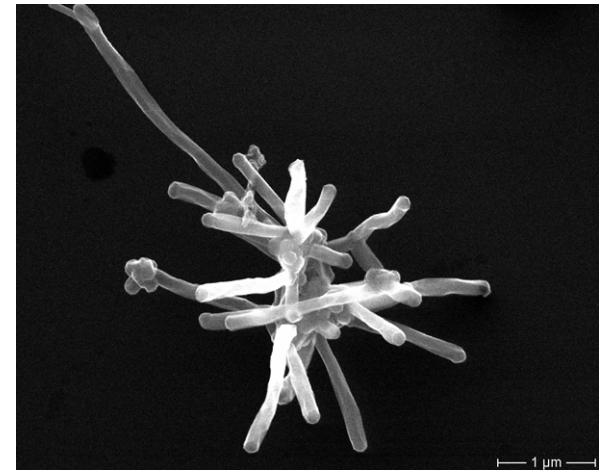


tangled

negative ip test

Muller et al., 2009 ($l=0.7\ \mu\text{m}$)

Nagai et al., 2011, 2013 ($l=3\ \mu\text{m}$)



rigid

positive ip test

Takagi et al. 2008

Nagai et al., 2011, 2013

Rittinghausen et al. 2014

positive inhalation test

Fukushima, yet unpublished

Side note: it would be a fatal error...

... to limit the focus
on nano
(<100 nm diameter)
only

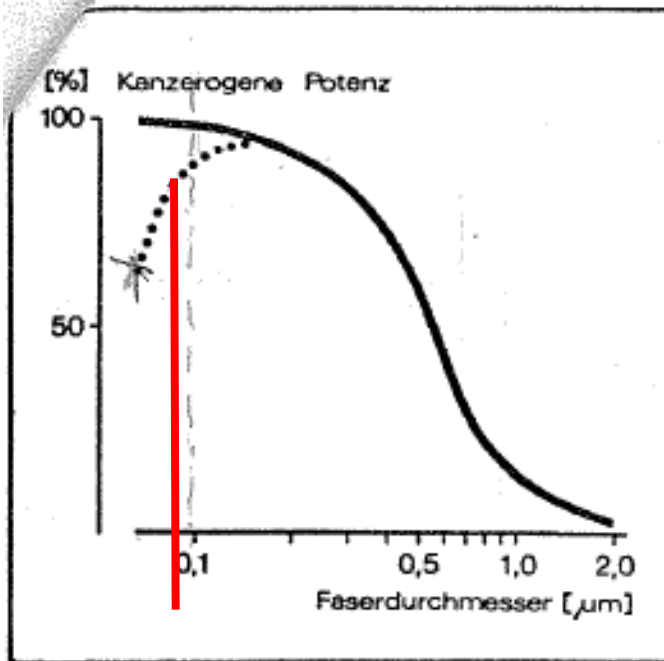


Abb. 4: Hypothese über die Abhängigkeit der kanzerogenen Potenz einer Faser vom Faserdurchmesser. (Bei konstanter Länge und gleichem Fasermaterial besitzen 5 Fasern von 1 μm Durchmesser etwa die gleiche kanzerogene Potenz wie 1 Faser von 0,5 μm Durchmesser.) Pott, ASP 8/77

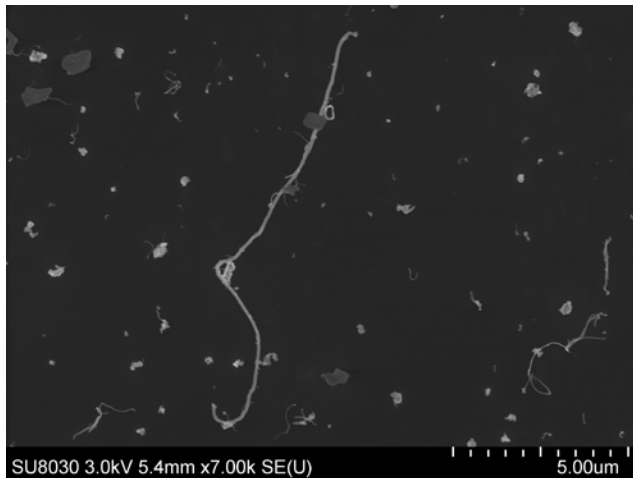
Example:
Biopersistent **respirable** fibres:
carcinogenic potency
and diameter

respirability up to $\sim 1\text{-}2$ μm median diameter

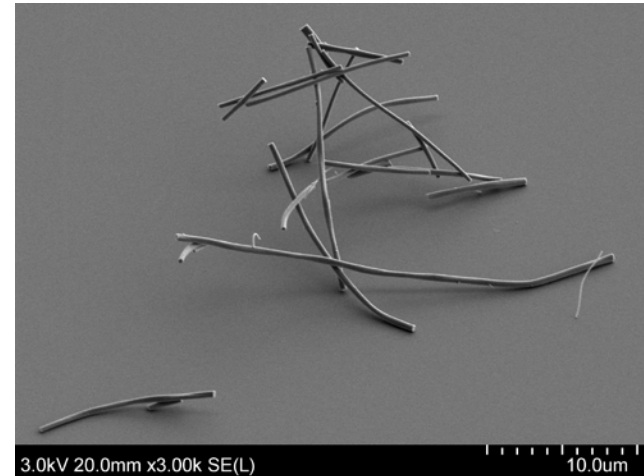
It is likely not only be restricted to MWCNT.....

CNTs, carbon fibres, nickel wires, silver wires, titanium dioxide fibres....

carbon fibres in use



Arry MWCNT



titanium dioxide

nickel nanowires

Toxic potency in comparison

reference values/OELs/cancer risk respirable dust (mass concentration)

	$\mu\text{g}/\text{m}^3$	category	critical effect
~10 ⁵	4 { 300 ¹	micro-GBP	threshold inflammation
	5 { 75 ¹	nano-GBP	threshold inflammation
	15 { ~15	quartz	threshold silicosis/lung cancer
	20 { ~1	crocidolite	cancer risk 4*10 ⁻⁴
	200 { ~0.05 to ~0.005	MWCNT	cancer risk 4*10 ⁻⁴ (assumption similar potency like crocidolite)

Summary

Critical fibres are highly potent carcinogens!

Past exposure and current occupational disease
asbestos

Current and increasing future exposure?
other biodurable fibres of WHO dimension

CNTs, carbon fibres, titanium dioxide fibres....

We have to take care **now**!