Wood dust

Evaluation of health hazards as basis for an occupational exposure limit

To: the minister of Work and Participation
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Collaboration of the Nordic Expert Group for
Criteria Documentation of Health Risks from Chemicals
and the Dutch Expert Committee on Occupational Safety,
a committee of the Health Council of the Netherlands

NEG THE NORDIC EXPERT GROUP

Health Council of the Netherlands

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Executive summary

Wood dust is released during wood processing such as sawing, sanding and milling. The particles can be inhaled via the airways and can cause health complaints. The Nordic Expert Group for Criteria Documentation of Health Risk from Chemicals (NEG) and the Dutch Expert Committee on Occupational Safety (DECOS) have evaluated the health hazard for occupational exposure to wood dust. Subsequently, health-based calculated occupational cancer risk values (HBC-OCRVs) have been derived. The HBC-OCRVs form the basis for the legal limits to be established by the Nordic regulatory authorities and the Dutch government to protect workers from harmful health effects from exposure to wood dust.

This advice was at the request of the Nordic authorities and the Dutch ministry of Social Affairs and Employment. More information on the task of the committees can be found at nordicexpertgroup.org and healthcouncil.nl.

Occupational exposure during wood processing

An estimated 3-4 million workers is occupationally exposed to wood dust in the European Union (EU). This represents about 2% of the EU workforce. The estimated numbers were highest represented in construction (1.2 million), furniture industry (700,000), builders' carpentry industry (300,000), and sawmilling (200,000). Occupational exposure also occurs in industries such as the forest industry and chemical and mechanical wood processing industries such as the pulp and paper industry.

The emission of wood dust and the inhaled concentration of the dust during work activities depend on various factors, e.g., woodworking processes and machining parameters, cleaning methods, types of wood materials, and dampness of wood. Sanding generally produces smaller particles than sawing and milling, sweeping the work area creates a higher concentration of wood dust in the air than vacuuming, and working with treated wood types such as MDF generates more wood dust than working with untreated wood types.

For wood dust, the main health effects occur in the upper respiratory tract. Therefore it is important to measure all particles that can be inhaled, i.e. the inhalable dust.

Evidence for a relation with cancer and nasal and respiratory symptoms

Exposure to wood dust is associated with various health effects and especially strong evidence exists for a relation between wood dust exposure and cancer and nasal and respiratory symptoms. The committees

concluded from epidemiological research that there is strong evidence for an exposure-response relation between wood dust exposure and nasal adenocarcinoma. Both direct and indirect genotoxic mechanisms have been reported as underlying mechanisms to wood dust carcinogenicity. For direct-acting carcinogens, it is assumed that each level of exposure poses some risk of cancer (non-threshold effect). The relative contribution of direct and indirect mechanisms of action to the carcinogenic effects of wood dust cannot be determined. Since a direct genotoxic mechanism of action seems to be involved, the committees decided to apply a risk-based approach and calculate HBC-OCRVs based on nasal adenocarcinoma.

The committees also concluded that there is evidence for an exposure-response relation between wood dust exposure and nasal and respiratory symptoms, such as coughing, throat symptoms, and sneezing, and with asthma development. However, the evidence for these respiratory effects does not allow the derivation of a reliable health-based recommended OEL.

Estimated HBC-OCRVs based on nasal adenocarcinoma

Only two studies were available that quantitatively express a relation between wood dust and cancer risk. The committees concluded that the study by Siew et al. (2017) is most suitable to calculate HBC-OCRVs. In this study, men were followed working in various wood-processing occupations in four Nordic countries. The subjects were exposed to both hardwood and softwood dust, but the exposure to softwood predominated. In this study, the wood dust exposure was estimated for 393 subjects with nasal adenocarcinoma and was compared to the estimated exposure of 1,965 subjects without nasal adenocarcinoma. Based on this comparison the committees determined an exposure-response relationship and calculated the following HBC-OCRVs:

- 4 additional cases of nasal adenocarcinoma per 100,000 workers (4×10^{-5}), for 40 years of occupational exposure, equal to 0.1 mg/m^3 (target risk level or low risk level).
- 4 additional cases of nasal adenocarcinoma per 10,000 workers (4×10^{-4}), for 40 years of occupational exposure, equal to 0.8 mg/m^3.
- 4 additional cases of nasal adenocarcinoma per 1,000 workers (4×10^{-3}), for 40 years of occupational exposure, equal to 2.9 mg/m^3 (prohibition risk level or high risk level).

The concentrations refer to the inhalable fraction, measured as the time-weighted average over an 8-hour working day. The committees note that respiratory symptoms can occur at exposure levels in the range of the HBC-OCRVs.

Recommendations apply to wood dust in general

Based on the available data on carcinogenic and genotoxic properties in both hardwood and softwood dust, the committees recommend to consider both wood dust in general as carcinogenic. The committees note that in practice, exposure often occurs to both hardwood dust and

softwood dust, and the applied exposure measurement methods do not distinguish between hardwood and softwood dust. Therefore, the committees' recommendations apply to wood dust in general.

Samenvatting

Houtstof komt vrij bij de bewerking van hout, bijvoorbeeld bij zagen, schuren en frezen. Het stof kan bij inademing in de neus en longen terechtkomen en gezondheidsklachten veroorzaken. De Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG) en de commissie Gezondheid en beroepsmatige blootstelling aan stoffen (GBBS) van de Gezondheidsraad hebben de gezondheidsrisico's van beroepsmatige blootstelling aan houtstof beoordeeld. Vervolgens hebben ze gezondheidskundige advieswaarden afgeleid. De advieswaarden vormen de basis voor door de Scandinavische regulatoire autoriteiten en de Nederlandse overheid vast te stellen wettelijke grenswaarden om werknemers te beschermen tegen schadelijke gezondheidseffecten van blootstelling.

Het advies is opgesteld op verzoek van het ministerie van Sociale Zaken en Werkgelegenheid (SZW) en de autoriteiten van Denemarken, Finland, Noorwegen en Zweden. Meer informatie over de adviesvraag en de commissies staat op gezondheidsraad.nl en nordicexpertgroup.org.

Blootstelling vindt plaats bij bewerking van hout

Beroepsmatige blootstelling aan houtstof vindt vooral plaats in de bosbouw, de bouwsector en de houtverwerkende industrie. Het aantal werknemers dat in Nederland wordt blootgesteld aan houtstof wordt geschat op 360.000. De hoeveelheid houtstof die vrijkomt en wordt ingeademd tijdens het werk is onder andere afhankelijk van het proces van verwerking, de manier van schoonmaken en het houttype. Zo veroorzaakt schuren in het houtbewerkingsproces over het algemeen kleinere deeltjes dan zagen en frezen, en zorgt het vegen van de werkplek voor een hogere concentratie aan houtstof in de lucht dan stofzuigen. Ook komt er bij het werken met bewerkte houtsoorten zoals MDF-platen meer houtstof vrij dan bij onbewerkte houtsoorten.

Voor houtstof geldt dat de belangrijkste gezondheidseffecten optreden in de bovenste luchtwegen. Daarom is het van belang dat alle deeltjes worden gemeten die ingeademd kunnen worden. Dit wordt inhaleerbaar stof genoemd.

Bewijs voor verband met kanker en luchtwegirritaties

Blootstelling aan houtstof wordt in verband gebracht met verschillende gezondheidseffecten. Er is vooral sterk bewijs voor het optreden van kanker en luchtwegirritaties. In epidemiologische studies is een verband gevonden tussen beroepsmatige blootstelling aan houtstof en een verhoogde incidentie van neuskanker (nasaal adenocarcinoom). Uit de

gegevens over houtstof blijkt dat houtstof zowel direct als indirect het DNA kan beschadigen. Voor carcinogene stoffen met een direct mechanisme wordt aangenomen dat elk niveau van blootstelling een bepaald risico op kanker geeft. In dat geval kan er geen veilige drempelwaarde worden afgeleid, maar wordt er een risicobenadering gehanteerd om het risico op kanker te beperken. De mate waarmee directe en indirecte werkingsmechanismen bijdragen aan de kankerverwekkende effecten van houtstof kan niet worden bepaald. Vanwege een mogelijke betrokkenheid van een direct genotoxisch werkingsmechanisme hebben de commissies besloten om risicogetallen te berekenen: advieswaarden die overeenkomen met een vooraf bepaald risiconiveau, zie kader.

Ook is bekend dat blootstelling aan houtstof kan leiden tot prikkels, beschadigingen of ontstekingen aan de luchtwegen zoals de neus, keel, luchtpijp of longen die kunnen leiden tot bijvoorbeeld keelpijn, hoesten, niezen, en de ontwikkeling van astma. De commissies zijn van mening dat er op basis van de gegevens over luchtwegklachten geen onderbouwde advieswaarde kan worden afgeleid.

Advieswaarden op basis van neuskanker

Er zijn slechts 2 studies beschikbaar waarin de relatie tussen blootstelling aan houtstof en het risico op kanker getalsmatig is uitgedrukt. De commissies concluderen dat de studie van Siew et al. (2017) het meest geschikt is om risicogetallen te berekenen. In deze studie werden mannen gevolgd die werkzaam waren in verschillende houtverwerkende beroepen in 4 Scandinavische landen. Er vond voornamelijk blootstelling plaats aan zachthoutstof, maar ook aan hardhoutstof. In deze studie werd de blootstelling aan houtstof geschat van 393 personen met nasaal adenocarcinoom en vergeleken met de geschatte blootstelling van 1.965 personen zonder nasaal adenocarcinoom. Op basis van deze vergelijking hebben de commissies een blootstellingsresponsrelatie vastgesteld en de volgende risicogetallen berekend:

- 0,1 mg houtstof/m^3, overeenkomend met 4 extra gevallen van neuskanker per 100.000 werknemers (het streefrisiconiveau) bij 40 jaar beroepsmatige blootstelling.
- 0.8 mg houtstof/m^3, overeenkomend met 4 extra gevallen van neuskanker per 10.000 werknemers bij 40 jaar beroepsmatige blootstelling.
- 2,9 mg houtstof/m^3, overeenkomend met 4 extra gevallen van neuskanker per 1.000 werknemers (het verbodsrisiconiveau) bij 40 jaar beroepsmatige blootstelling.

De concentraties zijn tijdgewogen gemiddelde concentraties over een 8-urige werkdag. De commissies merken op dat er bij de geadviseerde concentraties ook luchtwegklachten kunnen optreden.

Advieswaarden gelden voor houtstof in het algemeen

Op basis van de beschikbare gegevens over kankerverwekkende en genotoxische eigenschappen raden de commissies aan zowel hardhout-

stof als zachthoutstof als kankerverwekkend te beschouwen.
De commissies merken op dat in de praktijk blootstelling vaak plaatsvindt aan zowel hardhoutstof als zachthoutstof en dat de toegepaste meetmethoden geen onderscheid maken tussen hardhoutstof en zachthoutstof. Daarom gelden de de aanbevelingen van de commissies voor houtstof in het algemeen.

Risiconiveaus voor kankerverwekkende stoffen

Het ministerie van SZW heeft 2 risiconiveaus voor beroepsmatige blootstelling aan kankerverwekkende stoffen bepaald: het streefrisiconiveau en het verbodsrisiconiveau. Er wordt beleidsmatig gestreefd naar een grenswaarde die niet hoger is dan een concentratie die leidt tot 4 extra gevallen per 100.000 blootgestelde werkenden. Het verbodsrisico ligt een factor 100 hoger en stelt dat een grenswaarde nooit hoger mag zijn dan een concentratie die leidt tot 4 extra gevallen per 1.000 blootgestelde werkenden. Hierbij gaat het steeds om 4 extra gevallen van kanker door beroepsmatige blootstelling, dus bovenop het aantal gevallen door alle andere doodsoorzaken. Bij de berekening wordt er vanuit gegaan dat de werknemers gedurende hun gehele werkende leven (40 jaar) aan deze concentratie worden blootgesteld.

Preface

The current evaluation of Wood dust is a collaboration between NEG and DECOS. The main task of the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG) is to produce criteria documents to be used by the Nordic regulatory authorities as the scientific basis for setting health-based calculated occupational cancer risk values (HBC-OCRVs) for chemical agents. At the request of the Dutch Minister of Social Affairs and Employment, the Dutch Expert Committee on Occupational Safety (DECOS), a committee of the Health Council of the Netherlands, performs scientific evaluations on the toxicity of chemical substances that are used in the workplace. The purpose of these evaluations is to recommend HBC-OCRVs for the concentration of a substance in the air, provided that the data allows the derivation of such values. These recommendations serve as a basis in setting final, legally binding OELs by the Dutch and Nordic authorities.

NEG and DECOS have an agreement to collaborate in the evaluation and recommendation of HBC-OCRVs if a chemical substance is on the work programme of both committees. The committees both have permanent roles in giving scientific advice to help protect workers against the potentially harmful effects of chemical substances that they may encounter in the course of their work. In this connection, the committees assess the toxic properties and health effects of these substances and make recommendations for HBC-OCRVs. The joint advisory report can be used by the regulatory authorities in the Netherlands and in the Nordic countries when setting legally binding OELs. Additional information on the tasks of the committees can be found at gezondheidsraad.nl and at nordicexpertgroup.org. The members of the NEG and DECOS, and the consulted experts, are listed on the last pages of this advisory report.

This advisory report has been prepared by both the NEG and the DECOS. In November 2025, the president of the Dutch Health Council released a draft of this advisory report for public review. The comments received have been considered by the committees of both NEG and DECOS in deciding on the final recommendation and contents of this advisory report.
The comments and the replies can be found on the website of the Dutch Health Council.

Abbreviations

Abbreviation	Meaning
AM	arithmetic mean
BALF	bronchoalveolar lavage fluid
BEAS-2B	human bronchial epithelial cell line
BHR	bronchial hyperreactivity
BMI	body mass index
BOELV	binding occupational exposure limit value
CA	chromosomal aberrations
CHO	Chinese hamster ovary (cells)
CI	confidence interval
CMRD	Carcinogens, mutagens and reprotoxic substances directive (2004/37/EC)
COPD	chronic obstructive pulmonary disease
DRIFTS	diffuse reflectance infrared Fourier-transform spectroscopy
FAO	Food and Agricultural Organisation
FEV_1	forced expiratory volume in one second
FINJEM	the Finnish job exposure matrix
FVC	forced vital capacity
GM	geometric mean
GSD	geometric standard deviation
GSP	Gesamtstaubprobenahme filter sampler
HBC-OCRV	health-based calculated occupational cancer risk value
HPLC	high-performance liquid chromatography
HR	hazard ratio
HSE	Health and Safety Executive, UK
IARC	International Agency for Research on Cancer
IL	interleukin
IOM	Institute of Occupational Medicine, UK
IPF	idiopathic pulmonary fibrosis
ITAC	intestinal-type of sinonasal adenocarcinoma
LOAEL	lowest observed adverse effect level
LPS	lipopolysaccharides
MDF	medium density fibreboard
MIP	macrophage-inflammatory protein
MMAD	mass median aerodynamic diameter
MMEF	maximal mid-expiratory flow
MN	micronucleus
NACE	classification of economic activities in the European Union
NIOSH	National Institute of Occupational and Safety Health, US
NOAEL	no-observed adverse effect level
NOCCA	Nordic Occupational Cancer project
OEL	occupational exposure limit
OR	odds ratio
OVA	ovalbumin
PAH	polycyclic aromatic hydrocarbon
PB	particle board
PBL	peripheral blood lymphocyte
PCE	polychromatic erythrocyte
PEF	peak expiratory flow
$PM_{2.5}$	particulate matter 2.5 (µm)
PMNL	polymorphonuclear leukocytes
PVC	polyvinyl chloride
RIVM	Dutch National Institute for Public Health and the Environment
ROS	reactive oxygen species
RR	relative risk
SD	standard deviation
SCE	sister chromatid exchange
SCLC	small cell lung cancer
SCOEL	Scientific Committee on Occupational Exposure Limits
SEM	scanning electron microscopy
SSB	single-strand breaks
STAMI	Norwegian National Institute of Occupational Health
TGCT	testicular germ cell tumour
TNF	tumor necrosis factor
TWA	time-weighted average
VOC	volatile organic compound
WFI	wood fibre insulation board
WHO	World Health Organization

1 Introduction

Wood is one of the most important renewable resources in the world, and it is a widely used material all over. Out of the estimated 12,000 different species of trees, around 800 are softwoods, and the rest are hardwoods. It has been estimated that two-thirds of all wood used in the world is from softwood species.[92,93] Globally, approximately 2.2 billion cubic metres of wood is produced for industrial use, i.e. industrial groundwood, sawnlogs, veneer logs, and pulpwood. The production of the same wood items in the Nordic countries is approximately 150 million cubic metres.[57]

Occupational exposure to wood dust occurs in a wide variety of wood-related industries all over the world. It was estimated that the number of workers occupationally exposed to wood dust was around 3-4 million in the European Union (EU) in 2000-2003, that represented about 2% of the workforce in the EU. The estimated number of workers exposed to wood dust were highest in construction (1.2 million), furniture industry (700,000), builders' carpentry industry (300,000), and sawmilling (200,000).[103]

Occupational exposure to wood dust has been associated with multiple symptoms and adverse health effects. These include effects on the eyes, upper and lower respiratory tract as well as skin, with both non-allergic and allergic mechanisms involved.[191] In addition, occupational exposure to wood dust is associated with increased risk of cancer of nasal cavities and paranasal sinuses (sinonasal cancer), a rare type of human cancer.[92]

International Agency for Research on Cancer (IARC) evaluated the carcinogenicity of wood dust in 1995[92] and again in 2012,[93] resulting in classification of wood dust as a human carcinogen (IARC Group 1). While the first evaluation included a footnote indicating that the evaluation was based on marked increase of sinonasal cancer associated with exposure predominantly to hardwoods,[92] the updated evaluation in 2012 did not have such specification but classified wood dust from both hardwood and softwood species as carcinogenic to humans.[93]

In Europe, the exposure to hardwood dust is regulated by the Directive on the protection of workers from the risks related to exposure to carcinogens, mutagens or reprotoxic substances at work.[55] The binding occupational exposure limit value (BOELV) for inhalable hardwood dust was set at 2 mg/m^3 (8-hour time-weighted average, TWA).

This document is based on the publications retrieved from a systematic literature search for wood dust conducted and reported by the Dutch National Institute for Public Health and the Environment (RIVM) in 2021.[175] The search covered the literature published before May 2021.
This literature search was complemented to cover the publications from 2021-2024, and additionally some relevant older articles and study reports.

The literature covered exposures to hardwood and softwood dusts.
In addition to exposures to untreated wood dust, there may also be some exposures to dust of treated wood, such as impregnated wood.
The articles did not always clearly specify the quality of the dust, and often the dust was mixed wood dust.

2 Substance identification

An estimated 12,000 species of trees exist on the Earth. Trees have characteristic type of wood, and can be classified botanically in two groups: gymnosperms and angiosperms. Gymnosperms, having exposed seeds, are chiefly conifers and are generally referred to as softwoods. Angiosperms, having encapsulated seeds, are deciduous trees (i.e. trees which lose all their leaves for part of the year) and generally referred to as hardwoods. These classes can be further separated into orders, families, genera and species.[92,93]

Out of the 12,000 different species of trees, only about 800 are softwoods, but two-third of the wood used commercially worldwide belongs to the group of softwoods. Examples of the softwood are spruce, pine and larch of northern latitudes as well as cedar, cypress, hemlock and redwood. The hardwoods include deciduous trees such as ash, aspen, birch, beech, oak and cherry, as well as tropical trees such as the mahogany family and teak.[92] Nomenclature of some softwoods and hardwoods mentioned in this document is presented in Table 1.

The terms softwood and hardwood do not necessarily refer to the hardness of wood.[92,93] The density of wood varies considerably within each family, however, hardwoods tend to be denser. Softwoods also generally have longer fibres (Table 2). The hardness of the two groups overlaps somewhat.[92]

Table 1 Nomenclature of softwood and hardwood types mentioned in document.

Genus and species	English	Finnish	Swedish	Norwegian	Danish
Softwood					
Abies	Fir	Pihta	Ädelgran	Edelgran	Ædelgran
Cedrus deodara	Deodar	Himalajansetri	Himalaya-ceder		
Chamaecyparis	Cedar	Setri	Ceder, Ädelcypress	Sedertre	Ceder
Cupressus	Cypress	Sypressi	Cypress	Sypress	Cypres
Dyera costulata	Jelutong	Jelutong	Jelutong		
Larix	Larch	Lehtikuusi	Lärk	Lerketre	Lærk
Picea	Spruce	Kuusi	Gran	Gran	Gran
Pinus	Pine	Mänty	Tall	Furu	Fyr
Pseudotsuga menziesii	Douglas fir	Douglaskuusi	Douglasgran	Douglasgran	Douglasgran
Sequoia sempervirens	Redwood	Punapuu	Redwoodträ		Rødtræ
Thuja	Thua, arbor vitae	Tuija	Tuja	Tuja	Tuja
Thuja plicata	Western red cedar	Jättituija	Jättetuja	Kjempetuja	Kæmpethuja
Tsuga	Hemlock	Hemlokki	Hemlockgran	Hemlokk	Hemlock
Hardwood					
Acer	Maple	Vaahtera	Lönn	Lønn	Løn, Ahorn
Alnus	Alder	Leppä	Al	Or	El
Betula	Birch	Koivu	Björk	Bjørk	Birk
Carya	Hickory	Hikkoripuu	Hickory	Hickory	Hickory

Genus and species	English	Finnish	Swedish	Norwegian	Danish
Carpinus	Hornbeam, white beech	Valkopyökki	Avenbok	Agnbøk	Avnbøg
Castanea	Chestnut	Kastanja	Kastanj	Kastanje	Kastanje
Dacrydium cupressinum	Rimu, red pine	Maorinpihkatippio	Rimu		Rimo, rød fyr
Fagus	Beech	Pyökki	Bok	Bøk	Bøg
Fraxinus	Ash	Saarni	Ask	Ask	Ask
Gonystylus spp.	Ramin	Ramin	Ramin		
Juglans	Walnut	Pähkinäpuu	Valnöt	Valnøtt	Nøddetræ
Malus spp.	Apple	Omenapuu	Äpple	Epletre/apal	
Mangifera indica	Mango	Mangopuu	Mango	Mango	Mango
Platanus	Sycamore	Vuorivaahtera	Tysklönn	Plantanlønn	Valbirk, Ahorn
Populus	Aspen, poplar	Haapa, poppeli	Asp, poppel	Osp, poppel	Asp, Poppel
Prunus	Cherry	Kirsikkapuu	Körsbärsträd	Kirsebærtre	Kirsebærtræ
Pyrus communis	Pear	Päärynäpuu	Päron	Pæretre	
Salix	Willow	Paju	Pil, Vide	Piletre	Pil
Quercus	Oak	Tammi	Ek	Eik	Eg
Tilia	Lime, basswood	Lehmus	Lind	Lind	Lind
Ulnus	Elm	Jalava	Alm	Alm	Elm
Tropical hardwood					
Acacia	Acacia	Akaasia	Akacia	Akasie	Akacie
Acacia melanoxylon	Australian blackwood	Mustapuuakaasia			
Agathis australis	Kauri pine	Kaurimänty	Kauriträd		Kauri fyr
Alstonia scholaris	Pulai wood, Indian pulai	Aasiansaitanpuu			Pulai træ
Brya ebenus	Cocus wood	Mustapuu, eebenholtsi			
Chlorophora excelsa	Iroko	Fustikki (afrikaniroko)	Iroko	Iroko	Iroko
Dalbergia	Palisander, Rosewood	Palisanteripuu	Palisander	Palisander	Palisander
Dalbergia latifolia	East Indian rosewood				
Dalbergia melanoxylon	African blackwood	Itäafrikanmustapuu			
Dalbergia nigra	Brazilian rosewood	Brasilian ruusupuu, jakaranda			
Dalbergia retusa	Cocobolo				
Dalbergia stevensonii	Honduras rosewood	Hondurasin ruusupuu			
Diospyros	Ebony	Eebenpuu	Ebenholts	Ibenholt	Ibenholt
Distemonanthus benthamianus	Ayan, Nigerian satinwood				
Grevillea robusta	Australian silky oak	Kultasilkkipuu			
Hevea brasiliensis	Rubberwood	Kumipuu	Gummiträd	Gummitre	Gummitræ
Jacaranda	Jacaranda	Jakaranda	Jakaranda		Jacaranda
Khaya anthotheca	African mahogany	Ghanankaija-mahonki			
Machaerium scleroxylon	Bolivian rosewood	Bolivian ruusupuu			
Mansonia altissima	African black walnut				
Meliaceae	Mahogany	Mahonki	Mahogny	Mahogny	Mahogni
Ochroma	Balsa	Balsapuu	Balsa	Balsa	Balsa
Paratecoma peroba	White peroba				
Pericopsis elata	Afrormosia	Kongonafromosia	Afrikansk teak		Afromosi
Psidium guajava	Guava	Guava	Guava	Guava	Guava
Pterocorpus soyauxii	Padouk	Punaveripihkapuu	Padouk		Padouk
Santalum	Sandalwood	Santelipuu	Sandelträd	Sandeltre	Sandaltræ

Genus and species	English	Finnish	Swedish	Norwegian	Danish
Tamarindus indica	Tamarind	Tamarindipuu	Tamarind	Tamarind	Tamarind
Tectona grandis	Teak	Tiikki	Teak	Teak	Teak
Terminalia superba	Afara	Limbaketapani			
Triplochiton scleroxylon	Obeche	Länsiafrikan abassipuu (apachi)	Abachi	Abachi	

Table 2 Comparison of softwoods and hardwoods from IARC.[92,93]

Characteristic	Softwoods	Hardwoods
Synonym	Gymnosperms, conifers	Angiosperms, deciduous trees
Density, mean (range) (g/cm^3)	White (silver) fir 0.41 (0.32-0.71)	European beech 0.68 (0.49-0.88)
	European spruce 0.43 (0.30-0.64)	European oak 0.65 (0.39-0.93)
	Scots pine 0.49 (0.30-0.86)	
Fibres	Long (1.4-4.4 mm)	Short (0.2-2.4 mm)
Cell type	One (tracheids)	Various
Cellulose	~40-50%	~40-50%
Unit	β-d-Glucose	β-d-Glucose
Fibre pulp	Long	Short
Polyoses	~15-30%	~25-30%
Unit	More mannose	More xylose
	More galactose	
Lignin	~25-30%	~20-30%
Unit	Mainly guaiacyl	Mainly syringyl or guaiacyl
Methoxy group content	~15%	~20%
Extractive content		
Non-polar (e.g. terpenes)	High	Low
Polar (e.g. tannins)	Low	High

2.1 Chemical properties

Wood dust is a complex material with a composition that varies notably according to the species of tree being processed. It consists mainly of cellulose, polyoses and lignin, all having macromolecular structures.
In addition, wood dust contains a large and variable number of substances of lower relative molecular mass. These include non-polar organic extractives, polar organic extractives, and water-soluble extractives (Table 2).[93]

2.1.1 Macromolecular components

The major component of softwood and hardwood is cellulose, constituting approximately 40-50% of the wood material. Cellulose can be characterised as a linear polysaccharide built up of D-glucose units joined by ß(l-4) glycosidic linkages.[92]

Polyoses, also known as hemicelluloses, consist chiefly of five neutral sugar units: glucose, mannose and galactose (i.e., hexoses) and xylose and arabinose (i.e., pentoses). In addition, some polyoses contain uronic acid units. The amount of polyoses in dry wood material is higher in hardwood (25-35%) than in softwood (15-30%) (Table 2). The polyoses have much shorter molecular chains than cellulose. The chains are branched and can contain side groups. Softwoods such as European spruce and Scots pine have more mannose and galactose units than hardwoods such as European beech (Table 3).[92]

Table 3 Non-glucosic sugars in polyoses of some woods (%).[92]

Species	Mannose	Xylose	Galactose	Arabinose	Uronic acid	Rhamnose
European spruce	13.6	5.6	2.8	1.2	1.8 [a]	0.3
Scots pine	12.4	7.6	1.9	1.5	5.0	-
European beech	0.9	19.0	1.4	0.7	4.8 [a]	0.5

[a] 4-O-methylglucuronic acid.
- not reported.

Lignin is the third macromolecular component of wood. It is a branched and reticular polymer which consists of aromatic phenylpropane units joined by various linkages. The softwood and hardwood lignins are structurally different, especially regarding their contents of three basic building blocks: guaiacyl, syringyl and *p*-hydroxyphenyl units.
Most softwood lignins have guaiacyl lignin units and minor amounts of syringyl and *p*-hydroxyphenyl units. On the other hand, hardwoods consist of higher proportions of syringyl units.[92]

2.1.2 Extractives

Wood consists of, in addition to the structural components cellulose, polyoses and lignin, a large mixture of organic and inorganic compounds. Wood extractives are lower relative molecular mass organic compounds that can be extracted from wood with non-polar or polar solvents.
In addition, wood contains small amounts of inorganic components; 0.2-0.5% in temperate zone woods, and often much more in tropical woods. The most important inorganic components of wood are potassium, calcium and magnesium, and in some tropical woods, silicon.[92]

The mass fraction of extractives varies from 0.1-1% in trees of temperate zones to 15% or more in tropical wood. Some of the extractives may have toxic, irritant or sensitising properties, and they can protect wood against injury or attack. The extractives may significantly affect the properties of wood. Some examples of the wood extractives are listed in Table 4.[92]

Many of the extractives are volatile, e.g., the monoterpenes in softwood, and can be released into the workplace air during processing of fresh (green) logs. The content of the volatiles in wood material decreases over the time, and dried timber emits much less volatiles than fresh wood.[92]

Organic extractives are categorised by their structure in three groups: aliphatic, alicyclic and aromatic. Non-polar extractives of wood consist of mainly terpenes, fatty acids, resin acids, waxes, alcohols, sterols, steryl esters and glycerides. The polar extractives of wood generally comprise aromatic (phenolic) compounds, i.e., tannins, flavonoids, quinones and lignans.[92]

Carbohydrates and their derivates as well as alkaloids, proteins and inorganics comprise water-soluble extractives of wood. According to IARC, hardwood contains more polar extractives than softwood.[92]

Table 4 Examples of wood extractives.[92]

Extractive	Wood	Examples
Non-polar		
Monoterpenes	Softwood	α-Pinene β-Pinene Δ^3-Carene Limonene
Triterpenes	Softwood/Hardwood	β-Sitosterol
Fatty acids and waxes	Softwood	Linoleic acid
	Hardwood	Palmitic acid Stearic acid
Resin acids	Softwood	Abietic acid Pimaric acid
Phenolic acids	Hardwood	Para-hydroxy-benzoic acid Vanillic acid Syringic acid
Phenolic aldehydes	Softwood/Hardwood	Coniferyl aldehyde
	Hardwood	Syringaldehyde
Polar		
Tannins	Hardwood	Gallic acid
Flavonoids	Hardwood	Flavan Flavanonol Flavone
Quinones	Softwood/Hardwood	2,6-Dimethoxybenzoquinone
	Softwood	Anthraquinone
Lignans	Hardwood	Syringaresinol
	Softwood	Plicatic acid
Stilbenes	Softwood	Pinosylvin

2.2 Physical properties

Wood dust consists of wood particles generated in the processing of wood. In general, the size distribution of wood dust particles is wide. It depends on e.g., the type of wood, its water content, air humidity, and processing method and tools. Wood dust can be characterised by its moisture content. Dust of dry wood (moisture content below 15-20%) is less elastic than dust of moist wood.[93] The major portion of wood dust mass consists of particles with an aerodynamic diameter larger than 10 µm.[35,82,119,156] Li et al. noticed that 75% of the measured wood dust mass had a mass median aerodynamic diameter (MMAD) greater than 31.3 µm.[119] Very fine particles of less than 1 µm diameter were scarcely found in wood dust.[156]

Characterization of wood dust particles with aerodynamic diameters ranging from 2.47 to 72.9 µm using SEM and Energy-Dispersive X-Ray Analysis showed that the particles are irregularly shaped (rectangular prisms, spheres, cones and cylinders) and can be classified as non-spherical. Long, irregular, spiral and tear particles are typical from conifers and short, flat and compact particles are characteristic of non-conifers.[68]

Hardwood dust is typically finer than softwood dust.[35,156] In the study of Chung et al., the mean sizes based on particle number size distributions of typical softwood (pine) and hardwood (oak) dusts generated by sawing were 18.6 µm and 4.9 µm, respectively (Table 5). The mean sizes based on particle volume (mass) size distributions were 68.0 µm and 30.3 µm, for pine and oak, respectively.[35]

Table 5 Mean particle sizes of dusts generated by sawing and sanding (80 grit sanding paper).[35]

Type of distribution	Mean size (µm)	
	Pine	**Oak**
Sawing		
Number distribution	18.6	4.9
Volume (mass) distribution	68.0	30.3
Sanding		
Number distribution	6.6	8.0
Volume (mass) distribution	41.9	24.3

3 Occurrence, production and use

3.1 Wood industries

The forest industry covers chemical and mechanical wood processing industries, e.g., pulp and paper industry and manufacture of various wooden products. Industries which predominantly carry out mechanised processing of wood are sawmilling and planing of wood, manufacture of wooden boards, manufacture of builders' carpentry and joinery, manufacture of wooden containers, manufacture of other wooden products, and manufacture of furniture.[103]

Exposure to wood dust also occurs in forestry and construction industry, as well as building and repairing of ships and boats. The latter industries employ a substantial number of typical woodworkers such as construction carpenters, woodworking machine operators, sawyers, and bench carpenters. Teachers specialised in woodworking are also exposed to wood dust to some extent.[103]

3.2 Wood consumption in the Nordic countries and the Netherlands

The majority of the wood harvested and used in the production is soft-wood, i.e. pine and spruce in Finland, Norway and Sweden, but hardwood is more common in Denmark and the Netherlands. Some figures of wood consumption in the Nordic countries and the Netherlands according to the statistics of the Food and Agricultural Organisation (FAO) of the United Nations are presented in the Table 6. The figures are the sums of the wood products produced and imported.[57]

The percentages of softwood in roundwood, logs, pulpwood and sawn-wood in the Netherlands are unexpectedly high (74-90%), because a large part of the wood is imported. The percentage of softwood in the group of roundwood, logs, pulpwood is smaller in Finland (82%) than in Norway (98%) and Sweden (90%), but sawnwood is almost completely (99%) softwood in all the three countries. The pulpwood is more commonly hardwood, mainly birch, in Finland than in Norway and Sweden. Plywood is produced and used in higher amounts in Finland than in the other countries, but the use of the particle and fibreboards is the highest in Denmark.[57]

Table 6 Estimated wood consumption in the Nordic countries and the Netherlands.[57]

Country	Wood fuel (1,000 m^3)	Industrial roundwood, logs, pulpwood (1,000 m^3)	Wood chips and particles, wood residues (1,000 m^3)	Recovered post-consumer wood (1,000 tonnes)	Wood pellets and briquettes (1,000 tonnes)	Sawnwood (1,000 m^3)	Plywood and veneer sheets (1,000 m^3)	Particle and fibreboards (1,000 m^3)
Denmark	2,130 (65%/35%)*	2,345 (78%/22%)*	1,084	160	3,003	3,365 (73%/27%)*	396	9,650
Finland	9,538 (50%/50%)*	59,131 (82%/18%)*	16,264	699	578	11,607 (99%/1%)*	1,392	381
Netherlands	2,471 (22%/78%)*	922 (74%/26 %)*	1,113	2,077	2,808	2,942 (90%/10%)*	594	1,294
Norway	1,976 (31%/69%)*	11,901 (98%/2%)*	3,277	801	261	3,569 (99%/1%)*	160	771
Sweden	6,150 (49%/51%)*	77,706 (90%/10 %)*	19,039	1,500	2,139	19,641 (99%/1%)*	405	1,633

* coniferous (softwood) / non-coniferous (hardwood).

3.3 Wood working processes and dust emissions

The emission of wood dust and inhaled concentration of the dust during work activities depend on various factors, e.g., woodworking processes and machining parameters, cleaning methods, types of wood materials, and dampness of wood. There are three basic types of woodworking processes that produce dust: sawing, milling and sanding. Both scattering of wood cells and breaking out of whole cells or groups of cells (chips) occur in all three operations. The more cell scattering occurs, the finer dust particles are produced. Sawing and milling are mixed scattering and chip forming processes, whereas sanding is mainly cell scattering. Sanding produces finer dust than e.g., sawing and milling.[82]

The rate of dust generation increases with the energy associated with the process, e.g., when the speed of a machine tool increases, the dust generation also increases.[174, 235] For instance, machine sanding generates more wood dust compared to manual sanding.[92] High amount of wood dust can be released into the air when applying high energy consuming processes, because dust control measures, e.g., exhaust ventilation, at the emission source are often insufficient at workplaces.[221] Rautio et al. studied and modelled the influence of various CNC (computer numerical control) milling parameters, such as feed speed and rotation speed, tool diameters and angles, and number of milling edges, on the amount of dust emission. The most important factor for dust emission seemed to be the average chip

thickness, and the milling parameters should be chosen so that the average thickness is greater than 0.05 mm.[174]

Cleaning of the workplace, machines and products, with compressed air is an important cause of high wood dust emissions and workers' exposure. Dry sweeping is also known to result in high concentrations of wood dust in the air. In addition, bagging dust from dust extraction systems may cause high wood dust exposure.[73,123,221]

The dust emission can also depend on the type of wood, e.g., sanding and milling of medium density fibreboard (MDF) generates more wood dust compared to sanding or milling of natural solid wood.[35,91,174,221] As opposed to sanding and milling, sawing of MDF did not result in different inhalable dust concentrations than sawing of natural wood according to Chung et al.,[35] but in the pilot study of Hursthouse et al. higher dust concentrations were measured also during sawing of MDF compared to sawing of softwood.[91] Thermally modified, thermo-treated wood creates a larger amount of fine dust compared to similar but untreated wood.[155] Another study showed that planing of thermo-treated birch and beech caused higher dust emissions than untreated wood, and the same situation was observed in sanding process of birch wood.[150] Rautio et al. noticed some differences between different solid wood materials. In general, dust emission was higher in the milling of hardwood materials than in the milling of softwood materials.[174] Ojima used softwood (cypress) and hardwood (beech) which were sanded with a portable sander with three different coarseness of sandpapers. The softwood generated more dust (g/min) than hardwood.[156]

The dampness of wood and type of wood affect the amount of generated wood dust and thus the level of exposure.[82,233] The dryer the wood, the less plastic are the cells, and more likely they scatter leading to dust formation. Thus, the dust formation and the size distribution of wood dust depend on the features of wood and the type of woodworking method.[82]

In the Nordic countries, the exhaust air from woodworking machines must often be filtered and recycled back to workplace air because of energy saving reasons. It is easier to filter coarse particles than fine particles and therefore fine, respirable wood dust particles can accumulate in workplace and cause health problems. The standard Safety of woodworking machines. Chip and dust extraction systems with fixed installations. Safety requirements[30] gives in the chapter 5.6 Protection against hazardous substances e.g. the limit concentration of dust in the recirculated air. The residual dust content in the recirculation air shall not exceed 0.1 mg/m^3, and the concentration shall be monitored continuously and measured in the air duct. The recirculated air must not raise the wood dust concentration in workspace air to a level where the health of employees is endangered.

4 Measurements and analysis of workplace exposure

4.1 Occupational exposure monitoring

Exposure to wood dust is usually measured as the mass concentration of wood dust (mg/m^3) in a worker's breathing zone. The dust samples are collected by pumping air through a sampler which contains a pre-weighed filter, and the concentration is determined gravimetrically by weighing the filter or the filter and filter cassette after the sampling.

The potential adverse health effects of exposure to airborne wood particles depend both on the toxicity of the wood particles, and the size of the inhaled particles (particle aerodynamic diameter). The latter determines the depth of deposition in the respiratory tract. There is international agreement on three health-related aerosol fractions for measurement of dust particles in the workplace air: *inhalable*, *thoracic* and *respirable*.[28,94] The smaller the particles the deeper they can penetrate in the respiratory tract.

Internationally, the *inhalable* fraction (Figure 1) is most often sampled for measuring wood dust concentrations, because this fraction covers all particles that may enter the nose and mouth.[91,112,183,235]

The *thoracic* fraction is the mass fraction of inhaled particles penetrating beyond the larynx (Figure 1).

The *respirable* fraction is the portion of inhalable particles that are capable of entering the deepest part of the lung, the non-ciliated alveoli (Figure 1).

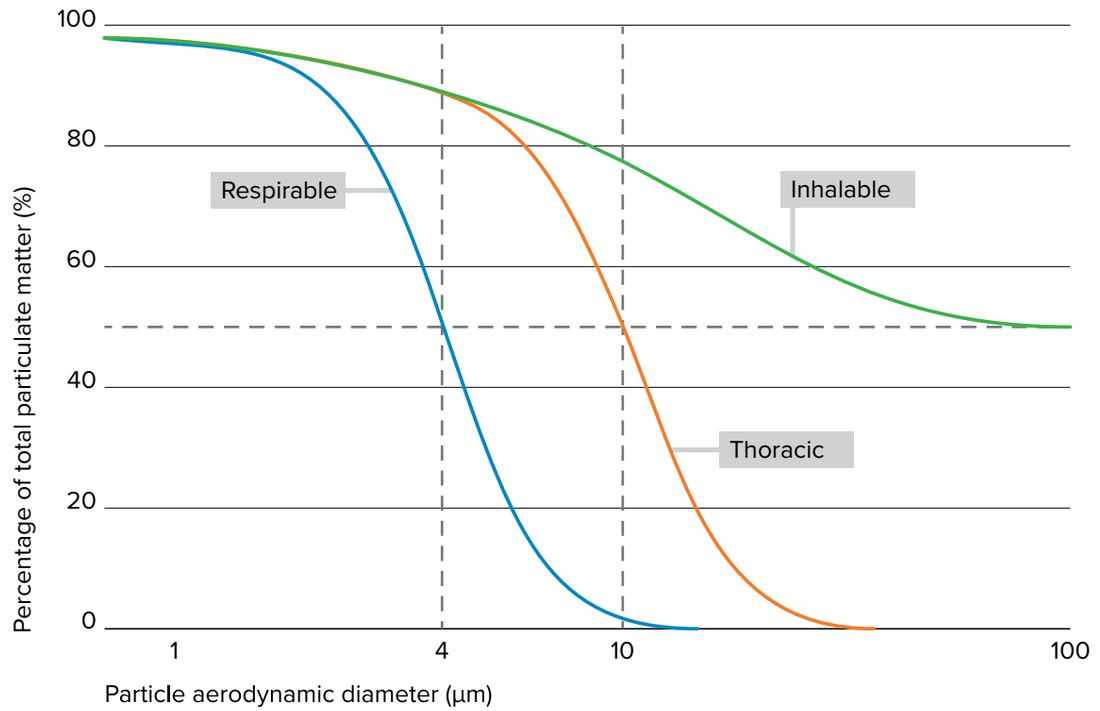

Figure 1 Percentages of total particulate matter for respirable, thoracic, and inhalable particle fractions based on standard EN 481:1993.[28] The vertical dotted lines mark the median diameters of respirable and thoracic particles.

4.2 Wood dust sampling

4.2.1 Inhalable dust sampling

The inhalable dust concentration is usually measured using active sampling, which means that the air is drawn over a sampler containing a preconditioned filter by using a pump. The sampling pump must be calibrated before and after sampling, and the sampling flow must meet the requirements set by the sampler so that the inlet air speed meets the conditions of the sampler. The sampling volume is the product of sampling flow and duration of the measurement.[177,183]

Vinzents and Schlünssen et al. have used passive sampling of wood dust in their studies. This method collects wood-dust on sticky transparent foils by diffusion. The amount of dust is determined by light extinction. The concentration of dust cannot be calculated, because the sampling volume is not known, and therefore this method must always be calibrated with the conventional active sampling method.[190,231]

Personal air sampling is conducted in the breathing zone of workers who carry dust samplers and pumps during a workday, up to 8 hours. The dust samplers for personal monitoring should comply with the internationally agreed inhalable dust conventions stated in the European standard EN 481:1993 Workplace atmospheres – Size fraction definitions for measurement of airborne particles[28] and the international standard ISO 7708:1995 Air quality – Particle size fraction definitions for health related sampling.[94] This makes it possible to compare results of various studies, and check compliance with occupational exposure limits (OEL).[177] There are also two other standards which need to be considered in dust sampling: EN 689:2018 Workplace exposure. Measurements of exposure by inhalation to chemical agents. Strategy for testing compliance with occupational exposure limit values[31] and EN 482:2015 Workplace exposure. General requirements for the performance of procedures for the measurement of chemical agents.[29]

Although the recommendations for wood dust sampling include sampling according to the inhalable dust convention,[117] and collecting inhalable wood dust is common in many countries, including the Nordic countries and the Netherlands, many different inhalable dust samplers are used. Sánchez Jiménez et al. published a review of monitoring methods for inhalable wood dust.[183] Table 7 is based on this review, and presents an overview of inhalable dust samplers and their ability to meet the international inhalable dust conventions.[28,94] All tested inhalable dust samplers meet the inhalable dust convention with the exception of the 37-mm cassette (both closed and open-face). The 37-mm cassette samplers collect the so-called total dust fraction, which is defined by the sampler itself and not by the inhalable dust convention.[214] However, there are critical aspects to be mentioned on all samplers. For example, external wind may result in under-sampling by PAS-6 and PERSPEC, and particles larger than 100 µm are over-sampled by

the IOM sampler. All the samplers are intended for up to 8 hours sampling.[106,120,183]

Conversion factors for total to inhalable dust

The 37-mm cassette samplers (sampling of total dust) were often used in the past, but are no longer considered to be adequate for capturing the most relevant particle size fractions regarding to health effects.

The studies summarised in the publication by Hagström et al. have shown that inhalable wood dust concentrations measured at workplaces are on average 1.5-4 times higher than total dust concentrations due to the different filter cassettes.[73] Eriksson et al. used conversion factor 2.5 for converting total dust concentrations to inhalable dust concentrtions in wood pellet industry.[53]

The open face 37-mm cassette was partly used for wood dust sampling in Finland until the end of 1990s. In 1994-1997, 120 parallel total dust samples and inhalable dust samples with IOM-samplers were collected from the workers' breathing zones at one sawmill, one plywood mill, and 12 manufactures of wooden products and furniture. The mass concentration ratios for the IOM/37-mm cassettes ranged from 0.05 to 20, the mean being 3.1 and median 2.2.[122]

The conversion factor from total dust to inhalable dust is always an approximation. The actual ratio can vary widely depending on many factors, such as the sampling method, type of wood dust, and particle size distribution of the dust being measured.

Table 7 Overview of dust samplers, their ability to meet the international dust convention and use in EU Member States.[177,183] All samplers are intended for dust sampling for hours, up to 8h.

Type of sampler	Sampling flow	Particles collected	Meeting CEN/ ISO curve for inhalable dust	Comments	Countries
37-mm cassette (closed)	2.0 l/min	Only on filter	No	Higher dust concentrations compared to 37-mm cassette (open) Large particles not effectively collected.	Past: Denmark France
37-mm cassette (open face)	2.0 l/min	Only on filter	No	Lower dust concentrations compared to 37-mm cassette (closed) Large particles not effectively collected.	Past: Finland Spain Sweden
Multi-orifice (seven-hole) sampler	2.0 l/min	Only on filter	Yes	May exhibit bias in some workplace conditions	UK (HSE)
IOM Inhalable sampling head	2.0 l/min	Both on filter and internal surface of the sampler	Yes	Over-samples large particles (>100 um)	UK (HSE) Finland The Netherlands
Button	4.0 l/min	Filter close to inlet, so minimal transmission losses	Yes	Low level Particulate Matter (PM) sampling	Unknown Finland (occasionally)

Type of sampler	Sampling flow	Particles collected	Meeting CEN/ ISO curve for inhalable dust	Comments	Countries
GSP Conical Inhalable Sampler (CIS)	3.5 l/min		Yes	May exhibit bias in some workplace conditions	Germany, UK (HSE)
CIP10 sampler version 2	10.0 l/min	No inner wall losses	Yes	CIP 10 version 1 showed some inner wall losses	France
PAS-6	2.0 l/min	Only on filter	Yes	External winds of 1 m/s result in under-sampling	The Netherlands
PERSPEC sampler	2.0 l/min	Both on filter and internal walls of the inlet nozzle	Yes	External winds of ≥0.5 m/s result in under-sampling	Italy (no longer commercially available)
RespiCon multistage particle sampler	3.11 l/min	Only on filter	Yes	Collects both inhalable, thoracic and respirable dust at one time	Unknown

4.2.2 Thoracic and respirable dust sampling

Although the inhalable fraction is generally considered to be the most important portion of wood dust, the thoracic and respirable wood dust fractions may also be sampled at workplaces, especially as a part of research.[206,207] Just as for measuring the inhalable fraction, measuring the thoracic and respirable fractions must comply with the thoracic and respirable dust conventions.[28,94] Thoracic and respirable dust are collected by active sampling using a pump which is connected to a wearable cyclone (i.e., the sampler). Many different cyclones are available for measurements of these dust fractions.

4.3 Analysis of dust samples

After sampling, the filters, or filters and filter cassettes are reconditioned to remove excess moisture, after which the mass of dust is determined gravimetrically. The dust concentration is determined by dividing the mass of inhalable dust by the sampling volume.

The limit of quantitation of inhalable wood dust concentration collected by the IOM-samplers was 0.1 mg/m^3 for a 1 m^3 sample.[180] Straumfors et al. used polyvinylchloride (PVC) filters and defined the limit of detection for thoracic dust 0.023 mg and inhalable dust 0.011 mg.[207]

Dust samplers collect airborne particles in the workplace air independent of their composition, and the gravimetric determination method may lead to overestimation of the inhalable wood dust concentration. A method has been developed based on spectroscopic analysis of the cellulose content, which is specific measurement of wood in the wood processing industry, and is largely unaffected by the presence of other potential particulate materials. The method uses diffuse reflectance infrared Fourier-transform spectroscopy (DRIFTS).[34,173]

In a Danish study, Vinzents and Laursen heated (4h, 480°C) samples collected in wood and furniture industry. The organic fraction of the dust was defined as wood dust and was measured gravimetrically as loss of mass after heating.[230]

The concentration of resin acids has also been used for separating wood dust from other dusts in dust samples collected at a lumber mill, and for estimating wood dust concentration. Resin acids are characteristic of wood, not of other dusts present in lumber mill environment.[215]

There is no standard analytical method to distinguish between hardwood or softwood dust. Identification of hardwood dust may be based on tannin content as hardwood dusts such as oak or mahogany have a higher tannin concentration than softwoods (e.g., pine, spruce, fir). The total tannin content cannot be used to identify the hardwood type since the tannin content also differs within wood species.[183]

Gallic acid (3,4,5-trihydroxybenzoic acid) and ellagic acid (2,3,7,8-tetrahydroxychromeno[5,4,3-cde]chromene-5,10-dione) have been reported as good indicators for oak dust. Oak, chestnut, and acacia have also shown high peaks of gallic, vanillic, ellagic and syringaldehyde acid, but not softwood species such as fir and spruce.[24,183] Carrieri et al. developed a method to identify teak wood dust via analysis of lapachol and deoxylapachol.[23]

4.4 Real-time dust monitoring

The result is the average concentration over the measurement period when determining the concentration of wood dust according to the standards EN 481:1993 and ISO 7708:1995.[28,94] Sometimes, it is necessary to also monitor the variation in dust concentration during the workday and identify the most exposing work phases and peak concentrations. In such cases, various direct-reading instruments can be used, most of which are photometers based on light scattering from particles. The intensity of the scattered light is proportional to the dust concentration.[73]

Such direct-reading dust monitors are widely available from a number of manufacturers. These instruments are predominantly designed to measure small particles in the respirable size range, although some particular monitors are claimed to be capable of measuring inhalable-sized particles. Thorpe noticed in his wind tunnel tests that direct-reading instruments based on light scattering underestimated the concentrations of the inhalable dust fraction.[218] Nitter Moazami et al. also found in their exposure chamber study that the total dust concentrations were underestimated.[141] Thorpe and Walsh studied direct-reading inhalable dust monitoring with several photometer-type monitors and monitors that combine photometry with particle measurement techniques during laboratory and field trials. Despite having limitations, the instruments showed promise as real-time inhalable dust monitors.[219]

The direct-reading dust monitors are calibrated by the manufacturers with standard test dusts, and the results may not accurately correspond to those of wood dust, which can have different density, colour, refractive index, and various shapes.[219] At present, these real-time monitoring instruments

cannot measure wood dust concentrations comparable to the occupational exposure limit values, but they can provide valuable information about exposure sources and the variation of dust concentration during the measurement period. They can be used for evaluating the efficiency of dust control measures and motivating workers by visualizing the variation of exposure, especially when combined with video recording of workers' activities, i.e., video exposure monitoring (VEM).[141,163,179]

5 Occupational exposure data

5.1 Number of workers exposed to wood dust in Europe

Occupational exposure to wood dust occurs all over the world, in a wide variety of wood-related industries. In the WOODEX study, Kauppinen et al. estimated that the number of workers exposed to inhalable wood dust (from both hardwood and softwood, including dust from chemically treated wood) in the EU in 2000-2003 was highest in construction (1.2 million), furniture industry (700,000), builders' carpentry industry (300,000), sawmilling (200,000), and forestry (150,000). The estimated numbers of exposed workers in manufacturing of wooden boards, wooden containers and other wooden products were 90,000, 60,000 and 100,000, respectively. The exposure assessment procedure integrated labour force data, company survey data, country questionnaire data and exposure measurement data. There were an additional 700,000 exposed workers in miscellaneous industries in which carpenters, joiners and other woodworkers were employed.[103]

Tiessink et al. reported that in the Netherlands approximately 360,000 workers were exposed to wood dust. Industries in which exposure to wood dust form an important risk for employees (approximately 100,000 workers) included the furniture industry, carpentry industry, timber trading industry and wood processing industry. In addition, in the construction industry approximately 135,000 workers are potentially exposed to wood dust.[221] It was not described in which industries exposure to wood dust takes place for the remaining approximately 125,000 workers.

A Swedish study estimated by the application of the job exposure matrix to national population registers, that approximately 100,700 workers were exposed to wood dust in Sweden in 2013. Most of them, 48,000 workers, worked in construction, and 26,200 workers in manufacturing tasks. The total occupationally active population in Sweden in 2013 was 4.4 million.[70]

In Finland, it was estimated that about 45,000 workers were exposed to wood dust in 2013-2015,[58] whereas the number was about 65,000 during the WOODEX study in 2000-2003 (103). About 7,000 workers, were estimated to be exposed to wood dust concentration above 1 mg/m^3.[58]

According to Statistics Finland, in 2023 there were approximately 28,000 employees in Finland working in the manufacture of sawn timber and wood and cork products (NACE 16), as well as in furniture manufacturing (NACE 31). Nearly every worker in these industries may be exposed to wood dust. The production of paper and cardboard pulp (NACE 1711) employs about

4,500 workers, and the construction sector (NACE F) employs about 182,800 workers, but only part of them are exposed to wood dust. The total employed population was 2.6 million in Finland in 2023.[205]

Due to the exposure to hardwood dust around 7,500 employees were reported into the Finnish Register of Employees Exposed to Carcinogens and Mutagens[102] in 2023.

5.2 Occupational wood dust exposure levels

In the WOODEX study detailed measurement data on wood dust were received from Denmark, Finland, France, Germany, and Great Britain, and some published data also from the Netherlands.[103] The data represented the wood dust concentrations over the period 1993-2002. Table 8 summarises these data by industries.[124]

Table 8 WOODEX exposure measurements grouped by country and industry.[124]

Industry	Geometric mean (GM)±geometric standard deviation (GSD) of inhalable dust, mg/m³					
	Denmark	**Finland**	**France**	**Germany**	**Great Britain**	**The Netherlands**
Sawmilling	1.0±3.2	0.9±3.5	0.6±3.7	1.4±3.4	1.4±5.0	-
Manufacture of wooden boards	1.7±3.4	0.4±4.1	1.0±3.6	1.2±3.0	-	-
Manufacture of builders' carpentry	0.7±2.5	0.8±3.7	0.8±2.8	1.5±3.2	2.6±3.1	1.6±2.0
Manufacture of wooden containers	1.5±2.6	-	1.0±3.2	1.8±3.4	2.2±3.6	-
Manufacture of other wooden products	2.7±3.8	0.7±4.3	1.4±3.2	1.3±3.6	3.3±3.8	-
Manufacture of furniture	0.9±2.1	1.2±3.7	1.4±3.3	1.3±3.6	3.1±4.1	2.9±2.8
Building of ships and boats	4.5±3.6	0.6±2.1	1.8±2.8	-	-	-
Construction	2.2±4.8	4.6±1.8	2.8±2.0	-	-	3.3
Forestry	-	-	-	0.1	-	-
Total number of measurements	**1,901**	**648**	**4,736**	**8,933**	**406**	**225**

Denmark: National Research Centre for the Working Environment (NFA) and studies by Schlünssen et al.[185,187,190]

Finland: Finnish Institute of Occupational Health.

France: COLCHIC database, INRS and CRAM France.

Germany: Holz-Berufsgenossenschaft, Munich.

Great Britain: Health and Safety Executive (HSE).

The Netherlands: studies by Scheepers et al.[184] and Spee.[203]

Inhalable particulates and isocyanates were measured in the European wooden board industry during manufacturing of oriented strand boards (OSB), MDF, wood fibre insulation boards (WFI), and particle boards (PB). The inhalable particles were collected by IOM samplers, and only the filters were weighed, not the filters and filter cassettes together. The authors named this particle fraction total inhalable particle (TIP), but it can be considered inhalable dust. The majority of the TIP was assumed to be wood dust. Totally, 446 samples were collected (283 personal samples and 163 background area samples). The samples had been collected during various work tasks and process areas, and the geometric means (GMs) of the personal samples varied between 0.25-0.93 mg/m^3 and of the area samples 0.10-1.34 mg/m^3.[226]

Lee et al. studied the performance of different dust samplers for personal wood dust exposure assessment in the wood products industry of the USA. Five samplers were tested, one total dust sampler (ACCU-CAP™) and four inhalable dust samplers (Button, CIP10-I, GSP, IOM). They collected in total 888 samples (444 valid pairs) in seven different wood industries manufacturing veneer, plywood, engine hardwood flooring, door skins, shutters, hardwood flooring, and kitchen cabinetry. The mass concentration of wood dust ranged from 0.02 to 195 mg/m^3. Geometric mean (GM)±geometric standard deviation (GSD) and arithmetic mean (AM)±standard deviation (SD) were 0.98±3.06 mg/m^3 and 2.12±7.74 mg/m^3, respectively. One percent of the samples exceeded 15 mg/m^3, 6% exceeded 5 mg/m^3, and 48% exceeded 1 mg/m^3.[117]

Gioffré et al. measured airborne microorganisms, endotoxins, and dust concentrations in two sawmills and four carpentry factories in South Italy. The measurements were performed in the different workstations over two working days. Altogether, 64 areal inhalable dust samples were collected by the IOM-samplers, and the arithmetic mean (AM) concentrations varied between 0.09-11.28 mg/m^3. The highest concentration was measured at the sanding station of one carpentry factory.[66]

Another Italian study examined 28 commercial chipping operations in order to determine operators' exposure to inhalable wood dust. The operations in energy wood chain were divided into industrial and small-scale operations. SKC Button samplers were used for personal inhalable wood dust sampling. In total 22 samples were collected in small-scale operations, 19 in industrial operations outside enclosed cabins, and 19 during working in the cabins. The mean (range) of inhalable wood dust concentrations were 1.08 (0.22-3.66) mg/m^3, 1.75 (0.19-10.24) mg/m^3 and 0.57 (0.07-3.93) mg/m^3, respectively.[127]

The temporal trend in wood dust exposure in the production of wood pellets was studied in Sweden during 2001-2013. Wood dust measurements were conducted in 14 production units which used

softwood. The inhalable dust samples were collected using IOM and GSP samplers, but also open-faced 37-mm filter cassettes had been used during 2001-2005. In order to make these total dust concentrations comparable with inhalable dust concentrations collected by the IOM and GPS samplers, the results were multiplied by 2.5. In total, there were 617 inhalable dust measurements, 328 personal and 289 area measurements. The GM±GSD of personal samples was 0.62±3.20 mg/m^3 and of area samples 0.37±4.40 mg/m^3. Modelling showed that the wood dust level in the pellet production had decreased from 6.4 mg/m^3 in 2001 to 1.0 mg/m^3 in 2013.[53]

Straumfors et al. studied workers' exposure to wood dust, microbial components, and terpenes at 10 departments of 11 Norwegian sawmills and planer mills, where the main wood species were pine and spruce. They measured both inhalable and thoracic dust concentrations by using 37-mm conical inhalable sampling cassettes and BGI2.69 cyclones with polyvinylchloride (PVC) filters. The number of inhalable wood dust samples was 112, and the GM±GSD was 0.72±2.6 mg/m^3. The number of thoracic wood dust samples was 501, and GM±GSD was 0.09±2.6 mg/m^3. The correlation between inhalable dust and thoracic dust was moderate (r_p = 0.41, p <0.001). The inhalable dust exposure was highest for workers involved in kiln drying and sorting of dry timber. The sorting of dry timber caused also high exposure to thoracic dust as well as maintenance works.[206,207]

Table 9 summarises the measurements collected from these published articles. Some wood dust data of Norwegian National Institute of Occupational Health (STAMI) and Finnish Institute of Occupational Health (FIOH) are also presented in Table 9. The data of STAMI are from the EXPO-register.[56]

The wood dust measurement data of the FIOH[59] were collected during the services conducted by the FIOH, i.e. the measurements have been done at the workplaces that have ordered surveys. Therefore, the inhalable wood dust concentrations do not necessarily represent all companies in the wood industry. Usually, only moderately large companies use the services of the FIOH, but the research project by Liukkonen et al. conducted wood dust measurements in the small firms manufacturing wooden products and furniture.[123] The wood dust concentrations measured in the breathing zones of the workers were somewhat higher (GM 0.79 mg/m^3) than the personal concentrations (GM 0.61 mg/m^3) in the FIOH data of 2017-2021. The number of wood dust measurements in FIOH data was higher in 2017-2021 (n=793) than in the previous five year period of 2012-2016 (n=326), concerning especially the manufacture of wooden products and furniture. However, the dust concentrations were in general at the same level in the both periods, the geometric mean of all the measurements was 0.70 mg/m^3 in 2012-2016 and 0.71 mg/m^3 in 2017-2021.[59] One probable reason for the increased number of the measurements was the new BOELV for hardwood dust in the EU.

Pedersen et al. investigated the significance of air circulation and other factors which have impact on workers' exposure to wood dust and related air contaminants in the Norwegian wood products industry. The inhalable softwood dust concentrations were lower (GM 0.30 mg/m^3) than the hardwood dust concentrations (GM 0.52 mg/m^3).[165]

Table 9 Occupational wood dust exposure concentration levels in Europe reported in studies published in 2010 or later.

Reference	Wood species	Industry	Fraction *Sampler*	Personal (P)/ Area (A)	Number of measurements	GM mg/m^3	GSD mg/m^3
Vangronsveld et al. (2010)[226]		Production of wooden boards (MDF, OSB, PB, WFI)	Total inhalable particulate (TIP) mainly wood dust	A	283	0.25-0.93	
			IOM sampler	A	163	0.10-1.34	
Gioffré et al. (2012)[66]	Hardwood	Sawmills	Inhalable *IOM sampler*	A	16	1.21-4.48 (AM)	
		Carpentry factories		A	48	0.09-11.28 (AM)	
Magagnotti et al. (2013)[127]		Chipping for energy wood	Inhalable *Button (SKC)*	P	60	0.57-1.08 (AM)	0.89-2.68 (SD)
Eriksson et al. (2017)[53]	Softwood	Production of wood pellets	Total dust (multiplied by 2.5=> inhalable dust) *Open-faced 37 mm filter cassette in 2001 for personal samples, and in 2001, 2004, 2005 for area samples*	P	328	0.62	3.20
			Inhalable *IOM sampler in 2004, 2005 for personal samples* *GSP sampler in 2011, 2012, 2013 for personal and area samples*	A	289	0.37	4.40
Straumfors et al. (2018, 2020)[206,207]	Pine, spruce	Sawmills, planer mills	Inhalable *Conical inhalable sampling cassettes (CIS)*	P	112	0.72	2.6
			Thoracic *BGI GK2.69 cyclones*	P	501	0.09	2.6

Reference	Wood species	Industry	Fraction *Sampler*	Personal (P)/ Area (A)	Number of measurements	GM mg/m³	GSD mg/m³
EXPO data, Norway 2010-2014[56]	Softwood and hardwood	All measurements	Total dust	P A	180 14	0.53 0.23	2.60 2.76
		Sawmilling and planning		P	63	0.49	2.44
		Manufacture of wooden products		P A	25 10	0.44 0.29	2.33 2.35
		Manufacture of building products		P	43	0.78	2.01
		Manufacture of furniture		P	18	0.53	1.60
FIOH wood dust data 2012-2016[59]	Softwood and hardwood	All measurements	Inhalable *IOM-sampler*	P A	136 190	0.70 0.29	2.71 3.24
		Sawmilling		P A	26 82	0.74 0.28	2.61 3.40
		Wooden boards industry		P A	67 53	0.52 0.20	2.36 2.57
		Manufacture of wooden products		P+A	22	0.32	2.83
		Manufacture of furniture		P+A	13	2.0	2.63
FIOH wood dust data 2017-2021[59]	Softwood and hardwood	All measurements	Inhalable *IOM-sampler*	P A	391 402	0.71 0.23	3.80 1.89
		Sawmilling		P A	133 129	0.88 0.33	2.72 3.10
		Wooden boards industry		P A	75 58	0.45 0.19	2.27 2.25
		Manufacture of wooden products and furniture		P A	131 89	0.61 0.18	2.54 2.84
Liukkonen et al. (2022)[123]	Mainly hardwood	Small firms manufacturing wooden products and furniture	Inhalable *IOM-sampler*	P A	167 124	0.79 0.18	2.19 2.34
Pedersen et al. (2023)[165]	Softwood		Inhalable *Conical inhalable sampler*	P	242	0.30	0.28-0.35 (95%CI)
	Hardwood			P	81	0.52	0.42-0.65 (95%CI)

6 Toxicokinetics

Upon inhalation, wood dust deposits in the respiratory tract. The site of deposition depends mainly on the size of the dust particles, and on the respiratory dynamics of the individual.[41,121] Larger particles tend to deposit mainly in the upper airways, whereas smaller particles deposit primarily in the central and small airways, and in the alveolar region. Also, other characteristics of the particles, such as hygroscopicity, electrostatic properties and shape, may impact the deposition pattern.[41]
The determination of particle deposition in the respiratory tract can be modelled using in silico tools.[42,116] However, in silico dosimetry modelling has not been applied specifically to wood dust particles, taking in to account their morphological characteristics.

The size range of wood dust particles may vary depending e.g., on the type of the wood and woodworking process applied (see Section 2.2). For most processes, however, a large fraction of the particles will be relatively large (>10 µm), and thereby deposit primarily in the nose and upper parts of the respiratory tract.

Tian et al. simulated nasal deposition of wood dust generated by sawing of pine and oak, using computational fluid dynamics. They found major particle deposition in the nasal valve region and in the anterior section of the middle turbinate. Pine dust (mean particle size 19 µm) had a higher deposition efficiency in the nasal cavity than oak dust (mean particle size 4.9 µm) since it comprised a higher proportion of larger particles.
The authors concluded that wood dusts comprising a large fraction of fine particles, such as those generated by sanding, may pass the nasal cavity and deposit in the lower parts of the respiratory tract.[220]

The primary sites of nasal wood dust deposition were next to the nasal mucocutaneous junction and in the anterior end of the middle turbinate, according to observations in woodworkers diagnosed with sinonasal cancer.[72]

The clearance of dust particles from the upper respiratory tract and conducting airways occurs largely by mucociliary clearance.[121]
Particles deposited in the anterior (unciliated) part of the nose are eliminated by physical means such as sneezing, wiping and blowing. Particle clearance from the unciliated part of the nose is slower than from the ciliated regions.[63] The main clearance mechanism of particles deposited in the alveolar region is phagocytosis by alveolar macrophages, and subsequent movement within alveolar and bronchial lumen into the conducting airways, followed by mucociliary clearance.[121]

There are studies indicating impaired nasal mucociliary clearance in woodworkers.[15,86,245] In a sparsely reported study of Özler and Akoglu, the

mean nasal mucociliary clearance time in non-smoking wood industry workers (n=25) was 16.7±2.71 min in comparison to 12.28±1.98 min in an age-matched control group (n=25). The authors also reported a correlation between duration of exposure to wood dust and increased nasal mucociliary clearance time in the wood industry workers.[246]

There is no indication that wood dust particles could transport or accumulate in secondary organs, as can be expected from their relatively large particle size. However, the natural or added chemicals in the wood maybe absorbed through the respiratory or digestive system (following mucociliary clearance of the wood dust) and cause local or systemic effects. Many of the wood dust extractives are volatile, and exposures mainly occur during processing of fresh (green) wood. Dried timber does not emit as much extractives as fresh wood, but the inner part (heartwood) of hardwoods and certain conifers is rich in extractives such as tannins,[92] which may enable occupational exposure during secondary wood processing.

7 Biological monitoring

Usually, wood dust exposure is assessed by measuring wood dust concentration in the air, i.e., by collecting dust samples in the breathing zone of workers and determining the dust concentration gravimetrically (see Chapter 4).

Mämmelä et al. developed a high-performance liquid chromatography (HPLC) method for biomonitoring of occupational oak dust exposure based on nasal lavage as a biomonitoring matrix. Gallic acid was chosen as the indicator compound. According to the authors further validation of the method was necessary, and prospective studies were needed to confirm the value of method for routine occupational health care.[145]

In practice, there are no useful biomonitoring methods for assessing the occupational wood dust exposure.

8 Mechanisms of toxicity

8.1 Asthma

It is poorly known, through which mechanisms wood dust exposure may affect the development of asthma. Different wood species may have different allergenic and toxicological potential due to their different chemical composition and protein content.[188] The knowledge relies partly on case reports or case series about occupational asthma and a few epidemiological studies.

It is considered that wood dust exposure can induce occupational asthma through sensitisation, which means that mechanisms are mostly immunological.[10,172] The specific inhalation challenge is regarded as the gold standard to demonstrate sensitiser-induced occupational asthma.

Western red cedar (*Thuja Plicata*) has been studied most extensively, because of its wide use in North America. Western red cedar differs from other wood species because of its unusually high content of extractives. The non-volatile fraction of Western red cedar extractives, consisting primarily of plicatic acid, has been demonstrated to induce asthma.[32] Interestingly, only one fifth of the patients had detectable amount of plicatic acid-specific IgE in their serum. The proportion of patients with either isolated or biphasic late asthmatic reaction was high (89.2%) in a study of 232 subjects with Western red cedar induced asthma.[33]

Frew et al. studied the immunological mechanisms among 11 patients with Western red cedar asthma, 7 patients with atopic asthma and 7 healthy subjects. This study confirmed that plicatic acid releases histamine from bronchial mast cells and basophils of most patients with Western red cedar asthma, but not from patients with atopic asthma.[62] In another study, specific challenge test to plicatic acid was performed in 17 patients, 9 patients having positive and 8 patients negative reactions. The late asthmatic reaction induced by plicatic acid was associated with an increase in sputum eosinophils.[154] Altogether, based on these findings on Western red cedar asthma, type I hypersensitivity is rare and usually other immunological mechanisms are likely to be involved.

Other wood dusts and other agents present in wood dust have also been described to cause asthma, but the underlying pathological mechanisms are not well-known. Obeche wood has shown to cause asthma through IgE-mediated type I hypersensitivity[75] and its main allergen, Trip s 1 has been identified.[107] Related to other types of wood dusts, for example, iroko, pine, spruce and beech, IgE-mediated sensitisation is not common.[176,188,200] Different low molecular compounds in wood dusts may affect airways

through irritative and sensitising properties (e.g., terpenes, terpene derivates like abietic acid, phenolic compounds, tannins, stilbenes, flavonoids, and glycosides).[188]

8.2 Other pulmonary effects

Exposure to wood dust is suggested to cause inflammation and irritation of the respiratory system, although the exact mechanisms are not well known. Oxidative stress is considered as one of the mechanisms by which wood dust exposure affects lungs and may induce lung function decline and development of chronic obstructive pulmonary disease (COPD) [described detailed in the Section 9.3[171,193]]. The role of oxidative stress is supported by a study of Kargar-Shouroki of 45 furniture workers and 45 office workers. Among the furniture workers, the mean concentration of respirable dust was high; 1.51 mg/m^3. After controlling for confounding variables, the biomarkers of oxidative stress, FVC, FEV_1, and FEV_1/FVC% predicted were associated significantly with wood dust exposure. The authors reported also significant correlations between the lung function parameters and the biomarkers of oxidative stress.[100]

In idiopathic pulmonary fibrosis (IPF), the key feature of pathology is dysregulated alveolar epithelial repair. Chronic injury to the alveolar epithelium through environmental exposures may be an important contributor to disease pathogenesis.[144] The knowledge about the mechanisms of wood dust exposure in development of IPF is scarce.[64]

It is, however, important to note that the major portion of wood dust mass consists of particles with an aerodynamic diameter larger than 10 µm, which are not reaching the alveolar level.[217]

8.3 Genotoxicity and cancer

Epidemiological studies (Section 10.4) show that there is a strong relationship between cumulative exposure (expressed e.g. as mg/m^3-years) to wood dust and nasal adenocarcinoma, and a weaker relationship between cumulative wood dust exposure and non-adenocarcinoma sinonasal cancer. The underlying mechanisms of genotoxicity and cancer may differ by the type of wood (softwood vs. hardwood). Intestinal-type of sinonasal adenocarcinoma (ITAC; epithelial tumor of the nasal cavity and the paranasal sinuses histologically resembling intestinal adenocarcinoma) appears to be more associated with exposure to hardwood dusts, whereas in countries processing mainly softwoods, the occurrence of sinonasal adenocarcinomas is lower and the relative amount of non-intestinal-type is higher. These differences can be due to the differential chemical composition (Section 2.1) or particle properties (Section 2.2) of the wood types.

Several mechanisms have been proposed to contribute to the detected effects, which may be due to primary (ROS production and DNA damage) or secondary genotoxicity (inflammation). In vitro and in vivo studies using wood dust or its chemical components (Section 9.3) do not give a clear

picture whether the detected carcinogenicity is due to primary or secondary genotoxicity. In vitro experiments have shown that the potency of different wood dusts in inducing DNA damage and inflammatory interleukins do not correlate, which suggests that the observed genotoxicity of the studied wood dusts is independent of the cytokine-induced inflammation.[20]

Primary genotoxicity can be induced by the wood dust particles or compounds released from the particles. Studying genotoxicity in vitro is challenging since wood dust particles do not dissolve in culture medium. Therefore in vitro studies mainly address the effects of extracts from the wood dust particles instead of the effects of the particles itself. Also the actual exposure depends on to whether and to what extent the wood dust (particle or extract) enters the cells.

In general, fine and ultrafine particles are known to cause ROS as such,[47] and it has been demonstrated that in alveolar macrophages pine dust stimulates the generation of ROS.[126,148] In vitro studies,[171,204] summarised in Section 9.3) indicate that the production of reactive oxygen species (ROS) can be partially responsible for the DNA-damaging effect of wood dusts or their chemical components. Hardwood and pine dusts were cyto-genotoxic and able to induce oxidative DNA damage in vitro in human bronchial epithelial BEAS-2B cells and there was an association with a delay of DNA repair resulting in accumulation of DNA lesions.[204] Exposure to pine, birch and oak dusts induces cytotoxicity and ROS production in BEAS-2B cells indicating that ROS-related mechanisms are involved in wood dust toxicity in human airway epithelial cells.[171]

Several studies in wood dust exposed workers ([27,65,175] summarised in Section 10.4) also support the role of oxidative stress in wood dust genotoxicity. Decreased levels of superoxidase dismutase were measured in wood dust exposed workers indicating antioxidant stress due to increase in ROS. The exposed workers also had increased levels of DNA and chromosomal damage in peripheral blood leukocytes as well as increased level of micronuclei in buccal cells.[175] An association was shown between wood dust and oxidative DNA damage (M_1dG adducts in nasal epithelium and urinary 15-F_{2t}-isoprostane)[27] and biomarkers of oxidative stress (15-F_{2t}-isoprostane and 8-oxo-dGuo) were significantly correlated with exposure to wood dust.[65]

ROS have been shown not only to damage cells by peroxidising lipids and disrupting DNA and proteins, but also to exert signalling functions and modulate gene transcription.[211] Enrichment of ROS damage-type mutations in ITAC has been detected using whole-genome sequencing of formalin-fixed paraffin-embedded tissue samples[198] and COX-2 expression, known to be induced by ROS, is often featured in ITAC.[85] Mutations in the tumour suppressor gene P53 have been associated with different types of cancers, and they frequently occur in wood dust related sinonasal cancer.[84]

Sinonasal adenocarcinoma patients with wood dust exposure showed increased point mutation burden compared to non-exposed patients indicating that short-term genotoxic effects of wood dust may accumulate over a longer time period.[198] Also chromosomal imbalances concerning regions carrying various tumour suppressor genes have been reported in association to the development of wood dust-related adenocarcinomas of the inner nose.[110]

Secondary genotoxicity, mediated by inflammatory reaction, is likely to contribute to the carcinogenicity of wood dust. One proposed mechanism is reduced clearance of particles from the sinonasal cavity, leading to mechanical irritation, inflammation, and increased cell proliferation.[125] To support this, increased nasal mucociliary clearance time has been reported in wood industry workers (Chapter 6). The idea of several contributing factors, such as local irritation, free-radical generation, and consequences of microbial contamination, was also suggested by Tátrai et al.[213]

Chronic inflammation is suspected to contribute to the initiation and progression in various cancers, and studies presented in Section 9.2 confirm that wood dust induces inflammatory response in lungs in vivo. Cellai et al. proposed that free radicals produced by inflammatory reaction as a consequence of wood dust could play a major role in the development of sinonasal cancer.[27] In addition to cancer, oxidative stress-mediated inflammation can, if continuously produced during a longer period of time, contribute to a wide range of systemic health effects such as cardiovascular and neurodegenerative diseases.

Dust particles may act as carriers for additives such as formaldehyde, arsenic and chromium which may be present in stains, fixatives, preservatives, binders or glues used in the wood industry. Exposure to hexavalent chromium and formaldehyde have been associated with development of cancer in the nasal cavity and paranasal sinuses.[93]

In conclusion, free radical production and inflammatory mechanisms related to particle accumulation in specific regions of the respiratory system contribute to the wood dust related carcinogenicity. Wood dusts can induce primary genotoxicity, mediated by ROS production and direct genotoxicity of specific wood dusts or their chemical components (natural or added) cannot be excluded.

9 Effects in animals and in vitro studies

9.1 Irritation and sensitisation

In a cumulative contact enhancement test, female guinea pigs (15/group) were exposed by closed epidermal application (Finn Chambers) to jelutong hardwood dust (20% in petrolatum; 24 h) at four applications (days 0, 2, 7, 9), with two injections of Freund's complete adjuvant (FCA) (day 7).
Statistically significant incidence of positive responses was observed in a challenge test (0.2, 1 and 6 mg; 0.3, 1.0, 4.0 and 12.5% in petrolatum; 24 h) at 72 hours for ≥0.2 mg and for ≥4.0% in petrolatum, with a clear dose-response. At the highest doses, 6.0 mg and 12.5% in petrolatum, respectively, 15/15 and 14/15 of the animals showed positive responses.
In a rechallenge after four weeks, the incidence of positive responses at 72 hours correlated with the concentration of jelutong dust applied (0.1-12.5% in petrolatum; 24 h). Statistically significant incidence of positive responses in the rechallenge was observed for ≥2.0% jelutong in petrolatum.
No signs of dermal irritation were observed in the range-finding tests.[136]

9.2 Effects of single and short-term exposure

Table 10 summarises identified studies on single and short-term wood dust exposure in experimental animals. All the identified studies focused on inflammatory effects in the respiratory tract after oropharyngeal aspiration or intratracheal or nasal instillation, as presented below.

Male C57BL/6 J mice (10-12/group) exposed to yellow pine dust ($PM_{2.5}$) by single oropharyngeal aspiration (0.28 mg/animal) showed mild to moderate acute bronchiolitis and alveolitis at one day post-exposure. The inflammatory response receded during the 84-day observation period.[199]

Male Sprague Dawley rats (5/group) exposed to respirable pine dust by single intratracheal instillation (15 mg/animal) showed inflammatory lung effects that persisted over the post-exposure observation period of one month.[213] The authors reported corresponding lung effects for cellulose dust.

Persisting pulmonary inflammation was also indicated for hardwood dusts after single intratracheal instillation in male rats (15/group; 50 mg/animal; follow-up 1-6 months) and male guinea pigs (8/group; 75 mg/animal; follow-up 2-3 months) in two scantly reported studies.[12,239]

Female BALB/c mice (8/group) exposed to birch or oak dust (0.0005 or 0.05 mg/animal; particle size ≤5 µm) by repeated intranasal instillation

(twice a week for 3 weeks) showed influx of inflammatory cells in lung tissue and bronchoalveolar lavage fluid (BALF), and increased cytokine and chemokine expression in the lungs at the higher dose at one day post-exposure. No inflammatory response was observed at the lower dose, or in animals exposed to titanium dioxide dust in corresponding particle size range and dosing.[147]

In a further repeated intranasal instillation study with oak dust (0.05 mg/animal; particle size ≤5 µm) on female BALB/c mice (8-9/group; twice a week for 3.5 weeks), the influx of inflammatory cells and cytokine and chemokine expression in the lungs was found to be more prominent in non-allergic mice than in mice with ovalbumin-induced asthma, indicating different lung responses to oak dust depending on the immunological status of the animals.[146]

In a scantly reported study focusing on nasal clearance half-times, repeated intranasal installation of beech dust (9 times; ~2.5 mg/animal/time) in female rats (7/group) caused inflammation in the nasal mucosa in all exposed animals.[37] Nasal inflammation in animals exposed by single intranasal instillation (~5 mg/animal) or by inhalation (600 mg/m^3 for 10 min, or 10×1 hour) was either lacking or for other reasons not addressed by the authors.

In conclusion, the intratracheal or nasal instillation and oropharyngeal aspiration studies consistently reported pulmonary inflammatory response in animals exposed to hardwood or softwood dusts by single or repeated administration. The early intratracheal instillation studies showed persisting pulmonary inflammation in the exposed animals, while in the physiologically more relevant oropharyngeal aspiration study, the inflammation was reported to subside during the post-observation period.

Table 10 Respiratory tract effects in experimental animals after single or short-term exposure to wood dust.

Wood species	Particle size	Exposure conditions	Exposed animals, observation period	Findings	Reference
Beech	MMAD 4-5 µm	Inhalation (600 mg/m^3 for 10-15 min or 10×1 h); intranasal instillation (~2.5 mg in saline; single and repeated (9 times) exposure)	Female F344 Fischer rats (7/group for repeated instillation, number for other groups not given)	Inflammation in nasal mucosa after repeated intranasal instillation (no further details given). Nasal clearance half-times: 233±52 min (inhalation, single exposure); 276±50 min (inhalation, repeated exposure); 216±180 min (instillation, single exposure); 415±180 min (instillation, repeated exposure).	37
Yellow pine	$PM_{2.5}$ fraction	Oropharyngeal aspiration; single; 0 (saline) or 280 µg/animal	Male C57BL/6J mice (10-12/group); sacrifice: 1 and 7 days after treatment for BALF analysis; 1 and 84 days after treatment for histopathology	Mild to moderate acute bronchiolitis and alveolitis in 9/11 animals at day 1. Minimal inflammatory changes in the lungs in 1/12 animals at day 84. No significant changes in BALF.	199
Pine (also cellulose and fibre-free pine extract)	Respirable; no data on particle size	Intratracheal instillation; single; 0 (saline) or 15 mg/animal (in 1 ml saline)	Male Sprague Dawley rats (5/group); sacrifice: 1 week or 1 month after instillation	Pine dust and cellulose (1 week): Alveolar and interstitial oedema with infiltration of neutrophils, lymphocytes, plasma cells and multinucleated giant cells with fibre-like foreign bodies in the cytoplasm in the lungs. Mild sinus histiocytosis in lymph nodes. Pine dust and cellulose (1 month): Alveolar granulomatous inflammation, thickened interstitium with lymphocytic foci, increase of argyrophilic fibres in interalveolar septa and lumina of bronchioli and alveoli. Non-specific sinus histiocytosis in lymph nodes. Pine extract (1 week and 1 month): No pathological changes in the lungs and lymph nodes.	213
Sheesham and mango	71-75% <9.1 µm; 28% <4.5 µm	Intratracheal instillation; single; 75 mg/animal (in 1.5 ml saline)	Male guinea pigs (8/group); sacrifice 60 days (4/grp) or 90 days (4/grp) after instillation	Disintegration of giant cells, centrilobular emphysema and slight fibrosis in the lungs at both time points (no further details given).	12
Hardwood (no further information on species)	No information on particle size	Intratracheal instillation; single; 0 (saline) or 50 mg/animal (in 1 ml saline)	Male Wistar rats (15/group); sacrifice: 1, 3 or 6 months after instillation	Cellular nodules (without collagen fibres), dust-laden giant cells, and epithelioid cells found in alveolar space (no further details given). Increased BALF fibronectin and lung collagen levels at 6 months. No significant changes in BALF cell differentials.	239
Birch and oak (also lipopoly-saccharides (LPS) and titanium dioxide ($TiO_{2;}$ ≤5 µm))	≤5 µm	Intranasal instillation; 2 times/wk for 3 wks; 0.5 or 50 µg/animal (in 50 µl saline)	Female BALB/c mice (8/group); sacrifice: 1 day after last exposure	Increased flux of inflammatory cells in lung tissue and BALF with increased cytokine and chemokine expression in lungs at 50 µg (no response at 0.5 µg). More prominent response with oak than birch. No significant change in bronchial hyperreactivity. No signs of lung inflammation after exposure to LPS or TiO_2.	147
Oak	≤5 µm	Intranasal instillation; 2 times/wk for 3.5 wks; 50 µg/animal (in 50 µl saline); ovalbumin (OVA) asthma model	Female BALB/c mice (8-9/group); sacrifice: day 25	Influx of inflammatory cells in lung tissue and BALF with increased cytokine and chemokine expression in lungs (more prominent for non-allergic mice). Decreased bronchial hyperreactivity and inhibition of OVA-induced IL-13 upregulation in allergic mice.	146

BALF: bronchoalveolar lavage fluid, IL: interleukin, LPS: lipopolysaccharides, OVA: ovalbumin, TiO_2: titanium dioxide.

9.3 Genotoxicity and production of reactive oxygen species

Table 11 summarises identified in vitro and in vivo studies on genotoxicity and ROS production of wood dust, wood dust condensates and wood dust extracts. Several in vitro studies have been reported, but in vivo studies on the genotoxic effects of particulate wood dusts were not identified. Different types of extracts have been tested in rodents.

9.3.1 In vitro studies

In the EU-funded research project WOODRISK (Grant agreement ID: QLK4-CT-2000-00573) human lung epithelial cell line A549 was exposed to seven wood dusts that had not been impregnated with wood preservatives and were not contaminated with endotoxins. The specific surface area (m^2/g) of the different wood dusts determined by liquid nitrogen adsorption was: beech 3.24; birch 2.89; MDF 2.17; oak 2.92; pine 3.26; spruce 3.02 and teak 3.07. DNA damage was assessed by the single-cell gel electrophoresis (comet) assay at concentrations 0, 10, 30, 100 and 300 µg/ml after 3- and 6-hour exposure. There was a statistically significant dose response for beech, teak, pine and MDF dusts after 3 hours and for MDF dust after 6 hours. There was no difference between hardwood dusts (beech, oak, teak) and softwood dusts (pine and spruce) after 3 or 6 hours.[20] It is noteworthy that most DNA strand breaks detected after 3 hours of incubation with wood dust had been resolved after 6 h of exposure. Longer time points of 24 and 48 hours were excluded due to high cytotoxicity.

Induction of DNA damage (by comet assay) and production of ROS were studied in human bronchial epithelial (BEAS-2B) cell cultures using unimpregnated, uncontaminated dusts from oak, padouk, pine and European silver fir. According to SEM (scanning electron microscopy) analysis, more than 60% of counted particles had geometric diameter <1 µm. Tested doses were 0, 5, 10, 50 and 100 $\mu g/cm^2$, but highest dose was excluded from further analysis due to >50% cytotoxicity. After 16-24 hours exposure the sub-cytotoxic dose of 50 $\mu g/cm^2$ induced ROS formation both as peroxide-related molecules and superoxide and the observed increase in ROS production was associated with DNA damage. Hardwood dusts and pine induced oxidised base accumulation, while DNA damage from fir consisted mainly of single strand breaks (SSBs) (204). Dose-dependency of the findings was not reported.

Induction of ROS production was studied in mouse macrophage (RAW 264.7) cells and human polymorphonuclear leukocytes (PMNL) using doses 0, 1, 10, 25, 50, 100, 500 and 1,000 µg/ml. Over 95% of the studied pine, birch and beech wood dust particles were below 5 µm in size as measured by an optical particle counter. Absence of bacterial contamination was confirmed. Production of intracellular ROS was measured at time points of 0, 5, 10, 15, 30, 45 and 60 minutes. The greatest formation of ROS was observed with pine dust; all tested doses between 10-1,000 µg/ml induced significant increase over control. Birch dust induced significant increase in ROS production with doses 50-1,000 µg/ml. The maximum ROS production

was achieved after 10 minutes exposure to doses 500 and 1,000 µg/ml. Beech dust did not induce significant increase in ROS production as compared to the control. Highest tested doses (500 and 1,000 µg/ml) of all tested wood dusts caused >50% cell death in the PMNLs.[148]

ROS production and inflammatory response was studied in alveolar macrophages of male Sprague Dawley rats using pine and heat-treated pine dusts. According to SEM analysis, more than 95% of analysed wood dust particles had diameter less than 5 µm. Dusts were tested negative for endotoxin contamination. Exposure for 4 hours with 200 µg/ml induced significant increase in intracellular ROS production compared to the untreated control cells. Dust from untreated pine induced a significantly stronger inflammatory response than dust from heat-treated pine. The study suggests that dust-induced ROS production (direct or cell-generated) mediates non-specific inflammatory reactions.[126]

Significant induction of ROS production was also detected in human bronchial epithelial (BEAS-2B) cells after exposure to unimpregnated, uncontaminated pine, birch and oak dusts. According to SEM analysis, more than 90% of the dust particles had geometric diameter less than 5 µm. Cells were treated with doses of 10, 50 and 500 µg/ml for 30 min, 2 and 6 hours. Pine dust induced significant production of ROS after 30 min and 2 hours of exposure with doses 10 and 50 µg/ml, and after 6 hours of exposure with dose 50 µg/ml. Birch dust induced significant production of ROS after 2 and 6 hours of exposure with dose 500 µg/ml. Oak dust induced significant production of ROS after 30 min and 2 hours of exposure with all tested doses. In addition, caspase-3 protease activity was increased in BEAS-2B cells after 2- and 6-hour exposure to each of the wood dusts studied. No significant differences in ROS production or caspase-3 expression were observed between cells exposed to hardwood or softwood dusts.[171]

Apoptosis, oxidative DNA damage and inflammatory effects of poplar and spruce wood dusts were studied in A549 human lung cells. The cells were exposed for 24 hours to 20 and 100 µg/ml of the $PM_{2.5}$ dust fraction collected on Teflon filters during simulated sawing of glued plywood panels. The majority (>95%) of the saw dust was composed by large particles in the mm size range, and the $PM_{2.5}$ range accounted for 12-36% of the total mass of inhalable particles (PM_{10}). Poplar wood $PM_{2.5}$ induced more apoptosis than spruce, and the release of pro-inflammatory cytokines (IL-6 and IL-8) was stronger for poplar. In contrary, slight induction of oxidative DNA damage was detected following exposure to spruce wood dust, but not poplar. The hydrodynamic diameter was higher for poplar wood than for spruce, and the number of particles <1 µm was about 75% for spruce wood dust compared to ≤20% in poplar wood dust. These differences can explain the results if higher number of spruce wood particles are able to enter the cell and nucleus and damage the DNA.[25]

Methanol extracts of beech and oak (doses 0.033, 0.1, 0.33, 1, 3.3 and 10 mg/ml) and pine (doses 1, 3.3, 10, 33.3 and 100 mg/ml) were tested in human embryonic lung (MRC-2) cells with and without metabolic activation with S9. Beech and oak induced chromosomal aberrations (CA) with doses 0.33 and 1 mg/ml but only in the absence of metabolic activator. In the absence of S9, the increase in the total number of CA was reported to be dose-dependent for both hardwood extracts ($p < 0.05$). Pine extract did not induce CA (244).

Human peripheral blood lymphocytes (PBL) were treated for 24 hours with extraction-drying condensates of Eastern white pine (doses 0.01, 0.1, 1, 10 and 100 µl/ml). All tested doses induced statistically significant increase in the percentage of CA and frequency of sister chromatid exchange (SCE). Positive correlations between dosage and the percentage of CA and frequency of SCE were also reported.[131] In contrast, red oak extraction-drying condensate showed no effects in CA test in PBL after 24 hours treatment with doses 0.01, 0.1, 1, 10 and 100 µl/ml. In comparison Southern yellow pine condensate was tested using two different concentrations (1x and 1,000x) in the same test conditions and it was noted that the 1x condensate induced CA and SCE while the more concentrated condensate did not. Chemical analysis of the condensates revealed that some of the chemical components were presumably lost during the lyophilisation process.[130]

Southern yellow pine extraction-drying condensates (doses 0.01, 0.1, 1, 10 and 100 µl/ml) were tested in Chinese hamster ovary (CHO) cells and in human PBL. The highest tested dose 100 µl/ml was excluded from analysis due to high cytotoxicity. Doses 0.01-10 µl/ml induced CA in CHO cells and doses 0.1-10 µl/ml in PBL, but no statistically significant effect was detected in the SCE assay.[133]

Similar extraction-drying condensates of Eastern white pine (doses 0.01, 0.1, 1, 10 and 100 µl/ml) were also tested in CHO cells. After 24 h treatment all tested doses induced statistically significant increase in the frequency of SCE, and all but the lowest tested dose induced significant increase in the percentage of CA. Positive correlation was reported between the dosage and the observed genotoxic changes.[134]

Same study approach and test doses (0.01, 0.1, 1, 10 and 100 µl/ml) were used for Douglas-fir extraction-drying condensate in CHO cells. Statistically significant increase in the percentage of CA was reported for doses 0.1-100 µl/ml as compared to the control cultures. In addition, all tested doses induced significant increase in the frequency of SCE.[132]

Salmonella typhimurium reverse mutation tests (not included in Table 11) showed weak positive or borderline effects for ash, beech, and oak extracts. Of several compounds isolated from wood, only quercetin and

Δ3-carene showed mutagenic activity as assessed by the *S. typhimurium* reverse mutation test.[92]

9.3.2 In vivo studies

Genotoxicity of aqueous, ethanol, or methanol extracts of untreated beech wood dust was studied after topical application in the nasal epithelium of male Wistar rats via nasal drip at three concentrations (0.5, 1 and 2 g equivalent dust/kg bw) three times, every 24 hour for 48 hours. Animals were sacrificed 24 hours after the last treatment and nasal tissue was examined for induction of micronuclei and DNA adducts. The two highest doses of ethanol and methanol extracts resulted in statistically significant induction of micronuclei, and the increase was dose dependent ($p<0.01$). No difference was detected in the DNA adduct levels between different treatments and controls. In contrast to the alcoholic extracts, the tested aqueous extract did not induce genotoxicity in the nasal epithelium.[149] Number of treated animals per exposure group or a justification for the applied dose levels is not clearly informed.

Kunming mice (5 male and 5 female/dose group) were exposed to water extract of Birch wood dust (doses 30, 20, 15, 10 and 7.5 g dust/kg bw) by intraperitoneal injection. Micronucleus frequency in the polychromatic sternum marrow cells was significantly higher in exposed animals compared to controls. Highest doses (30 and 20 g dust/ kg bw) of extracts from baked and steamed wood dust caused mortality resulting in exclusion of these dose groups from the final analysis. The remaining doses of extract from baked and steamed wood dust induced lower effect than extract from unbaked and unsteamed dust.[98] The ratio between poly-chromatic and normochomatic cells, which can be used to evaluate cytotoxicity of the exposure, was not reported.

9.3.3 Conclusions

Reported in vitro studies, conducted with dust, extracts or condensates from various wood species and using different cell lines, suggest adverse effects such as cytotoxicity, ROS production, DNA-damage, and chromo-somal aberrations. Based on the results, both particulates and the chemical components of wood dust induce genotoxicity, but the effect is often specific to the species of wood. Studies reporting effects of particulate wood dust are consistently showing strong ROS production, which in some studies is shown to be associated with DNA damage and release of cyto-kines. Most wood dust extracts resulted in a dose-dependent increase in the frequency of CA and SCE. To be noted is that in vitro testing has been conducted primarily with particle sizes comparable to the respirable fraction of wood dust, to facilitate their suspension in the exposure medium.

In vivo studies, conducted only with wood dust extracts, are too scarce to provide useful information on the genotoxic potential of wood dust or dose dependency.

There is no standardised method for wood extraction, and each study reports different extraction strategies contributing to differences in the reported data. Extracts contain wide range of chemical compounds, such as terpenes, phenols, lignans, quinones, tannins, flavonoids and paraffins, but it is not possible to determine which chemicals contribute to the reported genotoxicity. It is also unclear if the commonly used alcohol extraction methods reflect the release of toxic chemicals from wood dusts in the upper respiratory tract of humans or other mammals.

Table 11 Studies of genotoxicity and reactive oxygen species (ROS) production on wood dust and wood dust extracts in vitro and in vivo.

Type of wood dust / extract	Exposure conditions	Test system/animal model	Findings	Reference
In vitro studies				
Hard (**beech**, **birch**, **oak**, **teak**) and soft (**pine**, **spruce**) wood dust (>90% of particles <5 µm); **MDF** dust (<100 µm, mainly <10 µm)	10, 30, 100, 300 µg dust/ml (diluted in culture medium) for 3 and 6 h (in triplicate)	Human lung carcinoma A549 cell line	**Comet assay (DNA strand breaks):** 3 h: significant dose-response for beech, teak, pine and MDF ($p<0.01$); 1.2-1.4-fold increase at the top dose compared to controls. No difference between hard and soft woods. 6 h: significant dose-response only for MDF ($p<0.01$).	20
Hard (**oak**, **padouk**) and soft (**pine**, **European silver fir**) wood dust (>60% of particles <1 µm)	50 µg/cm^2 for 16-24 h (suspended in buffered salt solution and diluted in culture medium)	Human bronchial epithelial BEAS-2B cell line	**ROS production:** Statistically significant ($p<0.05$) ROS production for all tested wood dusts. **Comet assay (DNA strand breaks):** Statistically significant induction of DNA damage (hardwood dusts and pine induced oxidised base accumulation, European silver fir induced single strand breaks). The observed increase in ROS production was associated with DNA damage.	204
Hard (**Poplar)** and soft (**spruce)** wood dust ($PM_{2.5}$ fraction)	20 and 100 µg/ml (diluted in culture medium) for 24 h (in triplicate).	Human lung carcinoma A549 cell line	**Apoptosis:** Poplar wood induced dose-depended apoptotic effect. **Comet assay (DNA strand breaks):** Spruce wood dust (20 µg/ml) induced significant increase of oxidative DNA damage. **Pro-inflammatory cytokines:** Poplar wood dust (100 µg/ml) increased release of IL-6 and IL-8. Spruce wood dust (100 µg/ml) increase release of IL-6. Higher fold change (>2.5) was detected following exposure to poplar wood dust compared to spruce wood dust (<1.5).	25
Soft (**Pine)** and hard (**birch** and **beech)** wood dusts (>95% of particles <5 µm)	10, 100, 1,000 µg/ml (suspended in buffered salt solution) for 60 min	Mouse macrophage (RAW 264.7) cells and human polymorphonuclear leukocytes	**ROS production:** Pine dust (100 µg/ml) induced maximal ROS production in RAW cells. Birch dust produced dose-dependent increase in ROS production. Pine and birch dusts produced dose-dependent ROS production in human polymorphonuclear leukocytes, the response was faster than in the RAW cells. Beech dust did not activate formation of ROS.	148
Soft **(Pine)** wood dust, heat-treated pine dust (>95 % of particles <5 µm)	200 µg/ml in culture medium for 4 h (6 experiments, in duplicate)	Alveolar macrophages from male Sprague Dawley rats	**ROS production:** Significant increase ($p<0.05$) after exposure to pine and heat-treated pine dusts compared to untreated control cultures. Results suggest that pine dust-induced oxidative stress mediates the expression of TNF-α and MIP-2 in alveolar macrophages.	126

Type of wood dust / extract	Exposure conditions	Test system/animal model	Findings	Reference
Hard (**birch**, **oak**) and soft (**pine**) wood dust (>90% of particles <5 µm)	10, 50, 500 µg/ml (in culture medium) for 0.5, 2, 6, 12 and 24 h	Human bronchial epithelial (BEAS-2B) cell line	**ROS production:** Maximal induction of ROS production after 30 min of exposure to 50 µg/ml of pine dust (3.3-fold increase), after 2 h of exposure to 500 µg/ml of birch dust (2.1-fold increase), and after 2 h exposure to 50 µg/ml of oak dust (2.3-fold increase). No significant differences in ROS production or caspase-3 expression between cells exposed to hard or soft wood dusts.	171
Methanol extracts of untreated hard (**beech**, **oak)** and soft (**pine)** wood dust	0.033, 0.1, 0.33, 1, 3.3, 10 mg/ml (beech and oak) or 1, 3.3, 10, 33.3, 100 mg/ml (pine) +/-10% S9 for 24 h (in triplicate)	Human embryonic lung MRC-2 cell line	**CA test:** No dose-dependent increase in the total number of chromosomal and chromatid breaks in the presence of S9. Dose-dependent increase in the absence of S9 ($p<0.05$) with beech and oak wood dust extract but not with pine extract.	244
Eastern white pine (softwood) extraction-drying condensate	0.01, 0.1, 1, 10, 100 µl/ml (in culture medium) for 24 h (in duplicate)	Human PBL	**CA test and SCE assay:** All tested doses induced significant ($p<0.05$) increase in the percentage of CA and in the frequency of SCE.	131
Red oak (hardwood) extraction-drying condensate	0.01, 0.1, 1, 10, 100 µl/ml (in culture medium) for 24 h (in duplicate)	Human PBL	**CA test:** No statistically significant effects.	130
Southern yellow pine (softwood) extraction-drying condensate	0.01, 0.1, 1, 10, 100 µl/ml (in culture medium) for 24 h (in duplicate)	Human PBL and CHO cells	**CA test and SCE assay:** Significant differences observed between the test and control groups for all tested doses in the CHO cells and for the two higher doses in the PBL CA test. No statistically significant effects in the SCE assay.	133
Eastern white pine (softwood) extraction-drying condensate	0.01, 0.1, 1, 10, 100 µl/ml (in culture medium) for 24 h (in duplicate)	CHO cells	**CA test and SCE assay:** All tested doses induced significant ($p<0.05$) increase in the percentage of CA and in the frequency of SCE.	134
Douglas-fir (softwood) extraction-drying condensate	0.01, 0.1, 1, 10, 100 µl/ml (in culture medium) for 24 h (in duplicate)	CHO cells	**CA test and SCE assay:** Doses above 0.1 µl/ml induced significant ($p<0.05$) increase in the percentage of CA. All tested doses induced statistically significant ($p<0.05$) increase in the frequency of SCE.	132
In vivo studies				
Aqueous, ethanol, or methanol extract of untreated **beech** wood dust (hardwood)	0.5, 1 and 2 g of extracted dust/kg animal weight, 3 consecutive exposures via nasal drip with 24 h intervals	Male Wistar rats	**MN in nasal epithelial cells:** Methanol and ethanol extracts of beech wood dust gave dose dependent increase ($p<0.01$) in the frequency of micronucleated cells. **DNA adducts (^{32}P-postlabelling):** No statistically significant results detected following treatment with any of the beech wood solvent extracts.	149
Water extracts of **birch** wood dust (hardwood), steamed and baked compared to unsteamed and unbaked	7.5, 10, 15, 20 and 30 g wood dust / kg body weight via intraperitoneal injection 2 times with 24 h interval	Kunming strain mouse, male and female (10/ group)	Doses 20 and 30 g/kg bw of steamed and baked wood dust were lethal and doses were excluded from analysis. **MN in PCE of sternum marrow:** Unsteamed and unbaked wood dust extracts gave dose-dependent increase ($r=0.96$, $p<0.0005$) in the frequency of micronucleated PCEs. Steamed and baked wood dust extract showed significant increase in the frequency of micronucleated PCEs ($p<0.001$) but the effect was not dose dependent.	98

CA: chromosomal aberration, CHO: Chinese hamster ovary, IL: interleukin, MDF: medium-density fibreboard, MIP: macrophage-inflammatory protein, MN: micronuclei, PBL: peripheral blood lymphocytes, PCE: polychromatic erythrocyte, PM2.5: particulate matter with diameter <2.5 µm, ROS: reactive oxygen species, SCE: sister-chromatid exhange, TNF: tumour necrosis factor.

9.4 Effects of long-term exposure and carcinogenicity

Table 12 summarises identified studies on long-term inhalation exposure to wood dust in experimental animals.

Male Syrian golden hamsters (24/group) exposed to beech dust (~10 µm) at 30 mg/m^3 for 40 weeks (6 hours/day, 5 days/week) showed mild inflammation of nasal respiratory epithelium and stroma, with one animal showing metaplasia/dysplasia of the nasal epithelium and another one a nasal tumour. No histological changes in the nasal mucosa were detected in animals (12/group) exposed to 15 mg/m^3 for 36 weeks, or in the corresponding control groups. No exposure-related lesions were detected in the lower respiratory tract of the exposed animals.[49,236,237]

Pulmonary emphysema was observed in 5/15 female Sprague Dawley rats exposed to beech dust (~10 µm) at 25 mg/m^3 for 104 weeks (6 hours/day, 5 days/week) (0/15 in control group), without indication of tumours or squamous metaplastic or dysplastic lesions in the nasal cavity (0/15). In rats correspondingly exposed to formaldehyde (12 ppm), or to a combination of formaldehyde (12 ppm) and beech dust (25 mg/m^3), squamous metaplastic or dysplastic lesions in the nasal cavity were observed in 10/16 and 12/15 animals, respectively (0/15 in control group).[87]

No exposure-related nasal lesions or neoplastic lesions in the upper or lower respiratory tract were reported in male Wistar rats (15/group) exposed to beech dust (MMAD 7.2±2.2 µm) at 15 mg/m^3 for 26 weeks (6 hours/day, 5 day/week).[210]

Malignant lung tumours were observed in 2/51 of female Fischer 344 rats exposed to 18 mg/m^3 of oak dust (≤10 µm; mainly 2-7 µm) until natural death (4.5 hours/day, 5 days/week), in comparison to 0/96 in control animals. The statistical significance of this finding was not addressed by the authors. No tumours in the nasal cavity or exposure-related increase in non-respiratory tract tumours were indicated. A malignant nasal tumour was, however, observed in animals correspondingly exposed to oak dust treated with a sodium chromate stain (1/53), and in animals exposed to the sodium chromate stain only (1/49).[108]

Guinea pigs (5/sex/group) exposed to fir bark dust (MMAD 1.5 µm) at 1,143 mg/m^3 for 0.5 hours/day, 5 days/week for 24 weeks showed thickened interalveolar septa and perivascular inflammation in the lungs.[135]

A dermal carcinogenicity study on female Naval Medical Research Institute mice (70/group) exposed by skin application of a methanol extract of beech dust twice a week for 3 months (dose equivalent to 2.5-10 g dust/mouse/week), observed until natural death, indicated a dose-dependent increase in the incidence of skin squamous cell papillomas and papillomas and carcinomas combined (statistically significant trend).[93,142] The extract used in the study showed mutagenicity in Ames test with metabolic activation.

In conclusion, there are only a few long-term inhalation studies in experimental animals available on beech, oak and fir bark dust, and all of the studies have some methodological deficiencies, related e.g., to small number of animals (of one sex only), only one tested dose, and/or lacking details in reporting of the results. These deficiencies hamper drawing firm conclusions based on the studies. In one study on hamsters, nasal inflammation and lesions in the nasal cavity were reported for beech dust at 30 mg/m^3, but not at 15 mg/m^3, while the other studies, primarily on rats at 15-25 mg/m^3, did not indicate nasal lesions in the exposed animals. The only study on oak dust reported potential increase in malignant lung tumours in rats exposed at 18 mg/m^3, and in malignant nasal tumours for oak dust treated with sodium chromate.

9.5 Reproductive and developmental studies

No experimental data on reproductive or developmental effects of wood dust were identified.

Table 12 Long-term inhalation exposure studies on wood dust in experimental animals.

Wood	Particle size	Exposure conditions	Exposed animals, observation period	Findings	Reference
Beech	MMAD 7.2±2.2 µm	0 or 15 mg/m^3; 6 h/d, 5 d/wk for 6 months	Male Wistar rats (15/group); sacrifice: 18 months	No exposure-related lesions in upper or lower respiratory tract. No effects on body or organ weights.	210
Beech	70% ≤10 µm; 10-20% 5 µm	0, 15 or 30 mg/m^3; 6 h/d, 5 d/wk for 36 wks (0 and 15 mg/m^3) or for 40 wks (0 and 30 mg/m^3)	Male Syrian golden hamsters (12/group (0 and 15 mg/m^3) or 24/group (0 and 30 mg/m^3)	15 mg/m^3: No exposure-related neoplastic or other lesions. 30 mg/m^3: Mild inflammation of nasal respiratory epithelium and stroma (no incidences reported). Nasal tumour (1/22) and metaplasia/dysplasia of the nasal epithelium (1/22) (0/19-21 in controls). No exposure-related lesions in the lower respiratory tract.	49,236,237
Oak	0.4-10 µm; majority 2-7 µm	0 or 18 mg/m^3; 4-5 h/d, 5 d/wk for 25 wks or until natural death	Female Fischer 344 rats (58-115/group); sacrifice: 26, 34 or 45 weeks (3-5/time point), or until natural death	Lung tumours (adenocarcinoma and carcinoma) in 2/51 of exposed animals (0/96 in controls). Incidence of non-respiratory tract tumours did not differ between the groups. No exposure-related effects on body weight or survival.	108,109
Beech	70% ≤10 µm; 10-20% ≤5 µm	0 or 25 mg/m^3; 6 h/d, 5 d/wk for 104 wks; co-exposure with 12 ppm formaldehyde	Female Sprague-Dawley rats (16/group); sacrifice: 104 weeks	Beech dust only: Pulmonary emphysema in 5/15 of the exposed animals (0/15 in controls). No tumours or squamous metaplastic or dysplastic lesions in the nasal cavities (0/15). Incidence of non-respiratory tract tumours did not differ between the groups (details not reported). No exposure-related effects on body weight or survival. Formaldehyde only: Squamous metaplastic and dysplastic lesions in the nasal cavities (10/16; controls 0/15), with a squamous cell carcinoma (1/16; controls: 0/15). Beech dust with formaldehyde: Squamous metaplastic and dysplastic lesions in the nasal cavities (12/15; controls 0/15).	87
Fir bark	MMAD 1.5 µm	0 or 1 143 mg/m^3; 0.5 h/d, 5 d/wk for 24 wks	Guinea pigs (5/sex/group); sacrifice: 24 weeks	Marked oedema on the apex of the lungs, vascular granulation tissue on the pleural surface, lymphoid aggregates and perivascular inflammation in the lungs, thickened interalveolar septa (no incidences reported). No exposure-related effects on body weight, food or water intake.	135

MMAD: mass median aerodynamic diameter.

10 Observations in man

10.1 Effects of single exposure

Acute effects of exposure to air contaminants (wood dusts and volatile extractives such as colophony and terpenes) were studied on healthy volunteers. Lung function and concentration of interleukin 6 (IL-6) in nasal lavage fluid of 19 healthy volunteers (never worked with wood processing) were measured before and after 5-hour exposure in a sawmill sawing Scots pine. Ten volunteers had respirators equipped with THP2 particle filter and nine volunteer had respirators without a particle filter. The median concentration of total dust for subjects with and without the particle filter was 0.04 and 0.13 mg/m^3, respectively. The concentrations of endotoxin were below the detection limit (0.1 ng/m^3). There were no changes in spirometric values but a significant increase in the concentration of IL-6 in the nasal lavage was detected in the volunteers without the particle filter.[40]

10.2 Effects of short-term and long-term exposure

10.2.1 Nasal, eye and respiratory symptoms and signs

Schlünssen et al. performed a large workforce survey including 2,381 wood dust exposed workers from 54 Danish furniture factories. As a control, 619 persons without wood dust exposure were selected from three factories of other types of industries. Questionnaires were returned by 2,033 (88%) woodworkers and 474 (82%) controls, which comprised the final study population. Of the woodworkers 82% were male.[187] Exposure was assessed with measurements applying passive sampling of wood dust [described in Vinzents 1996[231] and Schlünssen et al. 2001[190]] among 1,579 woodworkers, and with a job-exposure matrix among 382 woodworkers. Calibration measurements were performed on 111 individuals using passive dust sampling alongside inhalable and total dust sampling. Linear regression models were used to convert passive dust measurements to inhalable and total dust concentrations. The arithmetic mean ± SD for the measured inhalable dust levels was 1.19±0.86 mg/m^3 and the range 0.17-9.78 mg/m^3. For total dust, the measured levels were 0.72-±-0.42 and 0.12-3.92 mg/m^3, respectively. Most workers (46%) were exposed to pine wood, while 30% were exposed to mixed wood types, 11% to particleboard, and 6% to hardwood. There was no indication of the use of impregnated wood in the study population. The exposures were divided according to inhalable dust concentration into low (0-0.74 mg/m^3), medium (>0.74-1.42 mg/m^3) and high (>1.42 mg/m^3) exposure category. Medium exposure was significantly associated with wheeze (OR 1.55, 95% CI 1.08–2.22), night wheeze (OR 2.15, 95% CI 1.15-4.02, and daily coughing (OR 1.40, 95% CI 1.08-1.82), in comparison to low exposure. High exposure was significantly associated with chest tightness (OR 2.22, 95% CI 1.00-4.93), night wheeze (OR 2.17, 95% CI 1.06-4.43), and daily coughing (OR 1.38, 95% CI 1.01-1.87). Also,

exposure to ≥1 mg/m^3 of inhalable wood dust was related to morning cough (OR 1.86, 95% CI 1.23-2.81), daily coughing (OR 1.42, 95% CI 1.06-1.90), and throat symptoms (OR 1.53, 95% CI 1.00-2.33), when compared with the controls never exposed to wood dust. Workers exposed to wood dust levels below 1 mg/m^3 only had an increased risk of morning cough (OR 1.61, 95% CI 1.06-2.43). There were no significant associations between wood dust exposure and self-reported asthma or chronic bronchitis.[187]

Schlünssen studied nasal effects using a sample of the same study population[185] as described above[187]. A total of 161 woodworkers and 19 controls participated. Most workers (39%) were exposed to mixed wood types, while 37% were exposed to pine wood, 17% to composite wood and 8% to hardwood. The workers having medium (0.74-1.42 mg/m^3) or high (>1.42 mg/m^3) exposure levels to inhalable dust had a significant increase in nasal congestion during the work shift, compared to before work. The multivariate linear regression analysis showed positive correlation between concentration of dust and change in mucosal swelling.[185]

Jacobsen et al. compared the studies of woodworkers from around 50 factories in Denmark in 1997-1998 (Study 1, the same population as described in Schlünssen et al.[187]) and in 2003-2004 (Study 2) using a similar type of exposure assessments in both studies. The median (range) level of inhalable wood dust was 1.0 (0.2-9.8) mg/m^3 in Study 1 and 0.6 (0.1-4.6) mg/m^3 in Study 2. There were 1 886 participants in Study 2; 78% of them were male and 55% non-smokers. Roughly, half of the study populations used softwood, 4-13% hardwood, 20% wood veneers and composite, and 14-20% other wood types. The participants reported less daily coughing (27.9% vs 32.8%), wheeze ever (17.8% vs 20.2%), chronic bronchitis (7.5% vs 9.5%), nasal symptoms (42.8% vs 48.8%), and conjunctivitis (7.3% vs 8.9%) in Study 2 compared to Study 1. On the other hand, the prevalences of self-reported current asthma and asthma ever were higher in Study 2 (5.1% and 8.2%, vs 3.9% and 6.2%, respectively). The decline in coughing, chronic bronchitis, and nasal symptoms from Study 1 to Study 2 were mainly explained by differences in the wood dust exposure level, and a dose-response relation was observed for coughing.[95]

Rongo et al. studied workers (n=546) of small-scale wood industries processing mainly hardwood species of African origin in Tanzania (teak trees, mahogany, and many other tropical trees, with some pine, cypress and other softwood species included). The breathing zone inhalable wood dust concentrations in these workshops ranged from 0.9-52.4 mg/m^3 (GM 3.9 mg/m^3) (based on 106 samples). An increased prevalence of respiratory symptoms was observed in the exposed workers compared with non-exposed office workers (n=565). A significant increase in symptoms such as cough; coughing up phlegm; awakened regularly because of cough; shortness of breath with wheezing; awakened by shortness of breath, runny nose, and sneezing more than once a week; itching and watering eyes; and allergy/sensitivity to house dust, food, animals, or

grasses/plants was demonstrated. High-exposure workers (GM 22.8 mg/m^3) and the low(er)-exposure workers (GMs 2.9-6.9 mg/m^3) seemed to have a slightly higher prevalence of symptoms compared with non-exposed workers, for instance, cough for low and high exposure together 50.7% and 39.5% for non-exposed, respectively. The overall eye irritation symptom prevalence was 4.8% in all exposed workers (n=546) (4.8% vs 2.1% in controls (n=565), adjusted OR 2.3, 95% CI 1.4-4.6), with a higher prevalence observed in workers with high exposure (n=131) (6.1% vs 2.1%; adjusted OR 3.0, 95% CI 1.2-7.8). The overall prevalence of itchy skin/skin rash symptoms in exposed group was 1.1% vs. 0.2% in non-exposed group (adjusted OR 6.3, 95% CI 0.8-52.2).[178]

Osman and Pala studied occupational exposure to wood dust and respiratory health in Turkish small-scale industry (328 woodworkers and 328 controls). The average total dust concentration was 2.04±1.53 mg/m^3. Most frequently used wood and/or wooden product types were MDF (68.6%; n=225), beech (11.6%; n=38), pine (10.4%; n=34) and fibreboard (6.1%; n=20). It was reported that 176 of workers (53.7%) had blocked nose while working, 141 (43.0%) redness of the eyes, 135 (41.2%) itching eyes, and 78 (23.8%) had runny nose, while no symptoms were observed in the control group.[158]

Bohadana et al. reported a slight increase in self-reported symptoms of runny nose and sore throat with increasing cumulative wood dust exposure (p=0.03-0.10) for 114 workers in five French wooden furniture factories processing mainly beech and oak. Cumulative exposure of the workers (as mg/m^3-years) was estimated and defined as the mean inhalable dust levels of different job categories (4-13 mg/m^3) based on breathing zone measurements in several wooden furniture factories.[16]

Holness et al. studied respiratory symptoms and nasal cytology in wood dust exposed (n=50) and control hospital workers (n=50) in Canada. Woodworking processes included sawing, sanding, assembly, laminating and gluing and miscellaneous, which included foremen and those in the shipping and receiving areas. Types of wood used in processes were not reported and thus unknown whether untreated or treated wood was processed. Respiratory symptoms were observed by questionnaire, and nasal cytology by nose swabs. Woodworker group's exposure to total dust was (mean±SD) 1.83±1.51 mg/m^3, and to respirable dust 0.29±0.31 mg/m^3. Control group's exposure to total dust was 0.43±0.38 mg/m^3, and to respirable dust 0.25±0.33 mg/m^3. More nasal and eye symptoms, cough, sputum and wheezing were reported in woodworkers than in control workers. In addition, more irritated cells were present in the woodworkers' nasal cytological smears.[88]

Andersen et al. studied Danish furniture industry workers (n=68) for respiratory symptoms and nasal congestion. During the study, 41 workers were occupied with machine- and hand-sanding and 27 with work such as

drilling, planing or sawing. The average breathing zone concentration of total dust in these two groups were 14.3 and 5.2 mg/m^3, respectively. Hard- and softwood were utilised: teak (hardwood) was most frequently processed, followed by oak (hardwood), chipboard and palisander, but mahogany, jacaranda, beech, ramin, motine, masonite and pine (softwood) were also processed. The most frequent complaints were dryness in the nose, eye irritation, nasal obstruction, prolonged colds and frequent headaches. Workers exposed to dust levels above 5 mg/m^3 more frequently experienced inflammation of the middle ear and common colds. No significant difference was reported in sinusitis, prolonged colds, asthma or troubles such as itching or bleeding nose, frequent sneezing and nasal obstruction. Prevalence of nasal congestion was reported to increase with increasing exposure levels: 1.0-2.9 mg/m^3: 11%; 3.0-4.9 mg/m^3: 25%; 5.0-6.9 mg/m^3: 31%; 7.0-9.9 mg/m^3: 46%; ≥10 mg/m^3: 63%. There was no connection between self-reported symptoms and the work performed, time of exposure or age.[7]

Borm et al. studied respiratory symptoms and nasal inflammation of 930 workers in an Indonesian woodworking plant processing mainly meranti wood. The workers were classified into three exposure categories (<2, 2-5, and >5 mg/m^3) based on their job titles and measured mean breathing zone inhalable dust levels in the different jobs. Exposure levels, cumulative exposure or years of employment were not associated with an increased prevalence of respiratory symptoms (self-reported cough, shortness of breath, wheezing, phlegm, bronchitis). Also, no relation was found between nasal inflammation (measured as nasal lavage cellularity) and estimated exposure levels or years of employment.[19]

Vedal et al. studied sawmill workers (n=334) in 8-hour work shift in Canada to observe short-term health effects of Western red cedar (softwood) dusts. The workers completed a respiratory-occupational questionnaire, in addition to total dust exposure assessments. Dust exposure ranged from undetectable to 6 mg/m^3 with a median of 0.2 mg/m^3. Exposure level of 1.0 mg/m^3 was exceeded by 10% of the workers and 4% of the workers exceeded a level of 2 mg/m^3. Symptoms of occupational asthma was reported by 52 workers, and it was more prevalent after 10 years of employment. In addition, chronic cough, phlegm, dyspnoea and persistent wheeze were reported without dose-dependency. Eye irritation symptoms were reported significantly more (31% vs. 8%) with exposure to dust concentrations of ≥2 mg/m^3 compared to <1 mg/m^3 exposure.[228]

Mandryk et al. studied effects of personal exposures on work-related symptoms of sawmill workers in three green mills i.e. milling fresh wood (n=53) and two dry mills i.e. milling dry wood (n=34) and controls (n=34) in Australia which mainly processed eucalyptus (hardwood). In addition, the levels of endotoxins were monitored. The mean inhalable dust level (range) at the green mills was 1.52 (0.25-74) mg/m^3 and at the dry mills 1.71 (0.55-11) mg/m^3. The mean (range) respirable dust levels were 0.19 (0.05-0.98) mg/

m^3 and 0.46 (0.28-1.05) mg/m^3 in the green and dry mills, respectively. Green mill workers had a significantly high prevalence of regular cough (50.9% vs. 29.4%), chronic bronchitis (37.7% vs. 11.8%), flu-like symptoms (35.8% vs. 17.6%), and eye irritation (49.1% vs. 29.4%) when compared to dry mill workers.[128,129]

Rusca et al. studied effects of bioaerosol exposure (wood dust, airborne bacteria, airborne fungi and endotoxins) on work-related symptoms among sawmill workers (n=111) in Switzerland (softwood). Twelve sawmills participated in the study and levels of bioaerosols, and symptoms were explored. The concentration of inhalable dust was in the range of 0.2-8.5 mg/m^3 with a mean of 1.7 mg/m^3. Workers with a short-term of employment (<5 years) reported more irritation symptoms (itching/running nose, snoring, itching/red eyes) than long duration employees. In addition, flu-like-syndrome was more frequently reported by junior workers. Workers with longer employment (>5 years) experienced more pulmonary symptoms (cough, wheezing, difficulty to breathe). Occurrence of pulmonary symptoms was associated with the level of airborne fungi.[182]

Górny et al. reported results from a questionnaire study assessing health effects among 28 workers of Polish wood pellet production facilities. Employees reported multiple adverse health effects including flu-like symptoms, respiratory symptoms (dry cough and wheezing 25%, cough with phlegm 13%), irritations (runny nose 13%, throat and skin irritation 13%, nose and eye irritations 38%). Wood dust concentration exceeding 3 mg/m^3 increased the probability of joint and muscle pains (OR 9, 95% CI 0.37-220.9) and nose and eye irritation (OR 3, 95% CI 0.15-59.9) as well as headache, heartburn and diarrhoea (OR 3, 95% CI 0.15-59.9).
Several background factors such as tobacco smoking, growing up or current residence on a farm, place of residence, type of the building and construction material and house pets were also reported to increase the probability of the adverse health effects.[69]

Pisaniello et al. studied personal inhalable dust exposures for woodworkers in 15 Australian furniture factories with survey of symptoms (controls n=46, softwood n=65, hardwood n=86, mixed n=168). Individual dust measurements were performed with mean exposures of 3.2, 5.2, and 3.5 mg/m^3 of inhalable dust for wood machinists, cabinetmakers, and chair frame makers, respectively. The dust concentrations gave a mean ratio of 0.14 (range 0.04-0.39) for respirable to inhalable dust. Woodworkers reported more eye, ear, and nasal problems compared with the control group. However, the prevalence of reported symptoms was poorly correlated with measurements of personal dust exposure, except for nasal symptoms. Hardwood users were more likely to report nasal symptoms (blocked nose 57% vs. 46%, sneezing 49% vs. 31%, runny nose 54% vs. 37%) than users of reconstituted wood when the mean TWA personal exposure was about 3 mg/m^3.[168]

Pisaniello et al. studied nasal cytological changes by using brush cytology in 50 male furniture workers (at least 10 years of work experience) and 50 controls in Australia. TWA exposure to inhalable wood dust was 0.5-15 mg/m^3 with a mean of 3 mg/m^3. A significant excess of cuboidal metaplasia (46% vs. 20% $p<0.05$) and a non-significant excess of squamous metaplasia (76% vs. 62%) was observed in woodworkers compared to controls. Cuboidal metaplasia was more frequent in woodworkers historically exposed to hardwoods and dust levels >2 mg/m^3, but the trend was not statistically significant. Also, the prevalence of frequent sneezing attacks (48% vs. 18%) and self-reported asthma ever (28% vs. 10%) was significantly higher in woodworkers compared to controls.[169]

In a study on Iranian furniture workers, wood dust exposed workers (n=45) reported more frequently respiratory symptoms such as wheezing (adjusted OR 5.89, 95% CI 1.68-20.66), sputum excretion (adjusted OR 5.83, 95% CI 1.69-23.27), and coughs (adjusted OR 9.76, 95% CI 1.14-83.99) ($p<0.01$) in comparison to non-exposed controls (n=45). There was no statistically significant difference in the incidence of self-reported asthma. Mean respirable dust concentration in the breathing zone of the exposed workers was high; 1.5±0.47 mg/m^3 (100). No information was given on the levels of total or inhalable dust.

In a Malaysian study among 241 furniture workers (high exposure: n=59; low exposure: n=182) exposed to rubberwood (*Hevea brasiliensis*) dust, workers in the high-exposure group showed significantly higher risks of nasal symptoms (OR 3.89, 95% CI 2.03-7.49) and eye symptoms (OR 2.63, 95% CI 1.41-4.91) compared with the low-exposure group. These differences were observed after workers reported respiratory symptoms via questionnaires. No statistically significant differences were found for cough, phlegm, chest tightness, breathlessness, wheezing, or skin symptoms. High exposure was also associated with significantly reduced lung function (FEV_1, FVC, FEV_1% predicted, FVC% predicted). Overall, rubberwood dust exposure above 1 mg/m^3 adversely affected upper-airway symptoms and lung function.[240]

In conclusion, the studies on woodworkers have reported wood dust to cause several different symptoms on nasal, eye and respiratory system compared to non-exposed controls (summarised in Table 13 in section 11.1) which were monitored mainly with questionnaires. All of the study designs were cross-sectional. The variety of upper airway symptoms reported were nasal congestion, blocked nose, runny nose, nasal irritation, sneezing, and sore throat. The reported eye symptoms included irritation, itching, redness and watering of eyes. Cough, wheezing, chest tightness, phlegm, dyspnoea, and irritation were reported as lower airway symptoms. The wood species, woodworking methods, exposure measurement methods, as well as the size of study populations, vary widely between the studies.

10.2.2 Skin irritation and sensitisation

Irritant dermatitis may arise from some timbers containing compounds with blistering properties due to histamine-liberating alkaloids.[76] Contact urticaria is rarely observed but may be produced by species such as obeche, ramin, teak and larch.

Estlander et al. reported allergic contact dermatitis and urticaria among wood dust exposed workers in Finland. During the period of 1976-1999, among the patients studied at the Finnish Institute of Occupational Health, allergic contact dermatitis was observed by patch/prick tests in 16 men, and 2 men had contact urticaria. The cases of allergic contact dermatitis were mainly associated with tropical hardwoods (teak, palisander, walnut, mahogany), Western red cedar, and pine dusts (colophonium), and the cases of contact urticaria to obeche dust. The authors concluded that wood dusts may cause occupational allergic skin dermatoses, both type I and type IV. In most cases, type IV allergic contact dermatitis develops from hardwood dusts but may also be caused by softwood dusts. The patients often had also mucosal symptoms, such as conjunctivitis, rhinitis and asthma. However, occupational allergic contact dermatitis from wood dusts was concluded to be relatively rare: During the period of 1990-1996, 24 (0.9%) out of 2,647 cases of allergic contact dermatitis, and 6 (0.5%) out of 1,205 cases of contact urticaria or protein contact dermatitis reported to the Register of Occupational Diseases in Finland were caused by wood species.[54]

10.2.3 Lung function changes

Noertjojo et al. studied the relationship between lung function and exposure to Western red cedar dust in an 11-year follow-up study of 243 sawmill workers compared to 140 non-exposed office workers (participants' sex ratio not reported). The workers reporting doctor-diagnosed asthma were excluded from the study. Cumulative exposure of the workers was estimated based on 1 132 personal and area total dust samples collected over 12 years, and the days the workers had worked in specific tasks.
The workers were classified into three exposure groups: low (average exposure <0.2 mg/m^3/day); medium (average exposure 0.2-0.4 mg/m^3/day); and high (average exposure >0.4 mg/m^3/day). Multiple regression analysis comparing the sawmill workers and the controls adjusted for age, race, height, initial lung function and smoking showed that sawmill workers had a significantly greater annual decline in FEV_1 and FVC (regression coefficients -12.1 ml/year, p=0.01 and -14.6 ml/year, p<0.05, respectively). Sawmill workers exposed to medium level of wood dust had a statistically significantly greater annual decline in FEV_1, being 16.9 ml as compared with the controls FEV_1, while decline of the workers exposed to high level remained non-significant (8.7 ml). The annual excess of forced vital capacity (FVC) decline was 15.8 ml among the workers exposed to medium level, and 21.3 ml among those exposed to high level of wood dust (both statistically significant compared to the controls). Thus, a dose-response relationship between the estimated exposure and the annual decline was seen in FVC which reached statistical significance in the medium and high

exposure groups (>0.2 mg/m^3/day).[153] However, no significant decline in $FEV_{1,}$ that is the most typical lung function change, in COPD was detected.

A 5-years longitudinal study on lung function changes in 1,164 wood dust exposed workers in 10 woodworking plants in the US did not show an association between estimated average wood dust, or total gravimetric dust, exposure and lung function changes in the exposed workers. Individual average wood dust exposure during the 5-years observation period was evaluated based on the job titles and a job exposure matrix (JEM) constructed using exposure measurement data from the corresponding plants. The GMs of inhalable, thoracic, and respirable dust in the plants were in the range of 0.77-2.5 mg/m^3 (inhalable), 0.15-0.54 (thoracic), and 0.10-0.23 mg/m^3 (respirable), and the mean percentages of wood solids in the dust samples 5.5-69% (inhalable), 7.5-91% (thoracic), and 2.3-34% (respirable). Plants processing Western red cedar and other allergenic wood species were excluded from the study, to allow for examining lung function changes not related to allergic asthma.[67]

Jacobsen et al. 2008 followed up Danish furniture workers for 6 years for the decline in lung function,[96] using a sample of the same study population as described in Section 10.2.1.[187] Later Bolund et al. reinvestigated the results using better standardised methods.[18] A total of 927 men and 185 women participated in the baseline and follow-up appointments in 1997-1998 and 2003-2005, respectively. Exposure was assessed as inhalable dust exposure level at baseline and as cumulative exposure during the follow-up period from a quantitative task specific job exposure matrix. Among females, an association was found between lung function decline and wood dust levels (p=0.005). The decline reached statistical significance in female workers exposed to >3.75 mg/m^3-years of inhalable wood dust during the 6-year follow-up period. An excess of FEV_1 loss during the follow-up was equivalent to 125 ml in females exposed to 3.75-4.71 mg/m^3-years in comparison to controls. Among male woodworkers, only smoking and asthma were significant predictors for new-onset COPD and excess decline in lung function.[18]

Schlünssen et al. 2004 studied the cross-shift changes in FEV_1 in relation to wood dust exposure[189] using the cohort described in their earlier study.[187] The percentage difference (cross-shift FEV_1) was calculated as pre-shift minus post-shift, divided by the largest measured FEV_1, multiplied by 100. The exposure to wood dust was calculated for each worker in eight different ways using individual measurements, group-based exposure estimates, a weighted estimate of individual and group-based exposure estimates, and predicted values of mixed models. Age-, gender-, and height-adjusted linear regression analysis on cross-shift decline in FEV_1 and dust exposure included 1,156 workers in total. A statistically significant positive association between dust exposure and cross-shift FEV_1 decline was revealed for non-smoking woodworkers for all but two exposure estimates. The group-based estimates using task and factory size as

grouping variable achieved the highest slope and standard error (SE) percentage decline in FEV_1 being 0.68 per 1 mg/m^3 dust, adjusted for age, gender and height. The lowest slope and SE were found for estimates based on individual measurements. Further stratification by pine revealed a stronger association for pine workers compared to woodworkers using other species, although statistical significancy was not demonstrated. No relation between dust exposure and cross-shift changes was seen for smokers. The authors concluded that there seems to be an association between average exposure to wood dust and cross-shift changes in FEV_1 among non-smoking woodworkers, especially among pine workers. Both individual and group-based approaches seemed to be relevant for exposure assessment.[189]

Jacobsen et al. 2013 studied, using the same cohort, both longitudinal and cross-shift changes in FEV_1 among 817 woodworkers and 136 controls in a 6-year follow-up study. The median (range) of inhalable wood dust exposure was 1.0 (0.2-9.8) mg/m^3 at baseline, while the cumulative exposure was 3.8 (0-7.1) mg/m^3-years. No significant differences were seen between woodworkers and controls of either sex in longitudinal and cross-sectional changes in FEV_1 and FVC. Interestingly, linear regression models adjusted for smoking, age, height and weight change showed no association between cross-shift and annual change in FEV_1 among woodworkers or controls. Including different exposure estimates, atopy or cross-shift change dichotomised or as quartiles did not change the results. The authors concluded that cross-shift change in lung function cannot be used to predict longitudinal changes in lung function among woodworkers exposed to relatively low levels of wood dust.[97]

Holness et al. studied cross-shift changes in respiratory function in wood dust exposed (n=50) and control workers (n=50) in Canada (described in detail in Section 10.2.1). Woodworkers' exposure to total dust was (mean±SD) 1.83±1.51 mg/m^3, and to respirable dust 0.29±0.31 mg/m^3. Controls' (housekeeping and maintenance workers at a hospital) exposure to total dust was 0.43±0.38 mg/m^3, and to respirable dust 0.25±0.33 mg/m^3. The woodworkers showed a significant decline over the work shift in FVC when compared to the controls (-2.36% vs -0.15%, p=0.005) and in FEV_1 (-2.47% vs 0.15%, p=0.005). No correlation was observed between the level of wood dust exposure and the observed lung function decline over the work shift. However, the workers' baseline FEV_1 as a percentage predicted (r=0.51, slope -0.91 % per mg/m^3-year, p=0.001) and FEF_{75} (0.52, -2.89, and 0.001, respectively) inversely correlated with the estimated cumulative exposure (measured respirable dust level×years of exposure).[88]

A cross-sectional survey of 1,157 US woodworkers exposed to dry maple or pine dust associated wood dust exposure with reduced lung function, with an indication of dose-response. The average total dust levels of the woodworking departments included were determined by stationary sampling close to workers' breathing zones, and the cumulative exposure of workers

(as mg/m^3-years) was estimated by multiplying these average levels by their employment years. The exposure was classified in three categories: low (<2 mg/m^3-years), medium (2-10 mg/m^3-years) and high (>10 mg/m^3-years), representing approximately 50%, 25% and 25% of the workers for both wood types, respectively. The ORs for reduced lung function, defined as the lower 5th percentile of the normal population, were 3.12 (95% CI 2.08-4.16, p=0.001) for FEV_1/FVC and 2.14 (95% CI 1.45-2.83, p=0.02) for the maximal mid-expiratory flow (MMEF) rate, when comparing high to low maple dust exposure categories. For pine dust, the corresponding ORs for high to low dust exposure were 4.03 (95% CI 2.30-5.76, p=0.001) for FEV_1/FVC and 2.45 (95% CI 1.48-3.42, p=0.02) for MMEF. The results were adjusted for age, hight, sex and smoking status of the workers.[234]

Badirdast et al. conducted a cross-sectional study on the lung function of 100 Iranian chipboard workers and 50 non-exposed controls. Chipboard workers' mean (±SD) exposure to inhalable dust, determined by breathing zone sampling, was 19±2 mg/m^3. There was no correlation between the level of dust exposure and the measured lung function parameters in age, height, and weight adjusted models. Instead, estimated cumulative exposure (multiplication of current exposure level with individual work history; mg/m^3-years) showed a statistically significant negative correlation with all the measured parameters (R^2 0.172 for FVC, 0.220 for FEV_1, 0.213 for FEV_1/FVC, and 0.235 for $FEV_{25-75\%}$, p <0.0001 for all variables).[9]

Bohadana et al. carried out a cross-sectional survey on the lung function and bronchial hyperresponsiveness of 114 workers in five French wooden furniture factories processing mainly beech and oak (described in detail in Section 10.2.1). No association was found between the studied lung function parameters (FVC, FEV_1, FEV_1/FVC, VE_{max50}, VE_{max25}) and estimated cumulative exposure. A bronchial challenge test with methacholine, however, showed a statistically significant association between bronchial responsiveness and cumulative exposure. An exposure-response relation was observed both for the proportion of subjects with a positive response (a fall in FEV_1 >20%) (p=0.002) and for the steepness of the dose-response of the observed hyperresponsiveness (p=0.014). No evident increase in the incidence of asthma or chronic bronchitis was observed among the exposed workers.[16]

Borm et al. carried out a cross-sectional survey on the lung function of 930 workers in an Indonesian woodworking plant processing mainly meranti wood (described in detail in Section 10.2.1). The workers were classified into three exposure categories (<2, 2-5, and >5 mg/m^3) based on their job titles and measured mean breathing zone inhalable dust levels in the different jobs. Also, cumulative exposure was evaluated based on the estimated exposure levels and the years of employment (median 17.5 mg/m^3-years, range 9-26 mg/m^3-years). There was no indication on reduced lung function (FVC, FEV_1, FEV_1/FVC, MEF, peak expiratory flow (PEF)) with increasing exposure levels or increasing cumulative exposure. Among male

workers (n=479), however, the years of employment had a negative association with FVC, FEV_1, FEV_1/FVC and MEF.[19]

Mandryk et al. studied effects of personal exposures on lung function in eucalyptus processing sawmill workers in three green mills (n=53), two dry mills (n=34) and controls (n=34) in Australia (described in detail in Section 10.2). The mean (range) inhalable dust level at the green mills was 1.52 (0.25-74) mg/m^3 and at the dry mills 1.71 (0.55-11) mg/m^3. The mean respirable dust levels were 0.19 (0.05-0.98) mg/m^3 and 0.46 (0.28-1.05) mg/m^3 and the mean inhalable endotoxin levels 6.61 (0.19-78.40) ng/m^3 and 1.58 (0.51-5.59) ng/m^3 in the green and dry mills, respectively. There was a statistically significant negative correlation between measured personal exposure to inhalable dust and FEV_1, FVC, and $FEF_{25-50\%}$. Dose-response relationship (Pearson's R) between percent predicted lung function indices, personal exposure, and number of years exposed were -0.30 for FEV_1, -0.27 for FVC, and -0.29 for $FEF_{25-50\%,}$ ($p<0.001$). Personal exposure to respirable dust was negatively correlated also with FEV_1/FVC. Additionally, inhalable endotoxin levels showed a negative correlation with FEV_1, FVC, and $FEF_{25-50\%}$ among green mill workers in the same magnitude as inhalable dust. The decline in FEV_1 was similar for inhalable dust and endotoxin (-0.36 vs -0.30% per year).[128,129]

Vedal et al. studied lung function in Canadian sawmill workers (n=334) exposed to Western red cedar (softwood) dusts (described in detail in Section 10.2.1). Total dust exposure ranged from undetectable to 6 mg/m^3 with a median of 0.2 mg/m^3. Exposure level of 1.0 mg/m^3 was exceeded by 10% of workers and 4% of workers exceeded level of 2 mg/m^3. FEV_1 and FVC were significantly lower in workers exposed to dust levels of ≥2 mg/m^3 than in those exposed to <2 mg/m^3. No association was observed between levels of $FEF_{25-75\%}$ or FEV_1/FVC and dust exposure.[228]

Thetkathuek et al. studied 685 workers in rubberwood furniture industry in Thailand. Twelve factories were randomly selected to the cross-sectional study and data was collected in 2007. The mean total dust level was 4.08 mg/m^3 (SD 1.42, range 1.15-11.17 mg/m^3). Sanding departments had highest levels of wood dust exposure. The authors reported a negative correlation between mean dust exposure level and FVC as well as FEV_1/FVC, but not for FEV_1. However, the statistical analyses of this study remained unclear and therefore conclusions are difficult to conduct.[216]

A cross-sectional study on lung function of 45 Iranian furniture workers indicated reduced lung function (FVC, FEV_1, and FEV_1/FVC) in the exposed workers compared to 45 non-exposed controls. Mean (±SD) respirable dust concentration in the breathing zone of the exposed workers was 1.5±0.47 mg/m^3.[100]

In the study of Andersen et al., no difference in FEV_1 or $FEF_{25-75\%}$ was found between Danish furniture industry workers (n=68) exposed to wood dust concentrations above or below 5 mg/m^3.[7]

Osman and Pala studied occupational exposure to wood dust and respiratory health system in Turkish small-scale industry (328 woodworkers and 328 controls, described in detail in Section 10.2.1). The mean FEV_1 and FVC values of woodworkers, among both smokers and non-smokers, were significantly decreased. However, FEV_1/FVC value was higher in the exposed group compared to the controls referring to restrictive type of lung function decline. A healthy worker effect was suggested.[158]

Zaman studied exposure to Pulai wood and lung function among 90 workers in pencil slat industry in South Sumatera Province of Indonesia. The mean (range) inhalable dust exposure in personal sampling was 0.1 (0.002-2.5) mg/m^3. A total of 23.3% of the workers had abnormal spirometry. Multivariate analysis including age, height, smoking status, and estimated cumulative exposure to wood dust (working duration×measured exposure level) showed no significant correlation between cumulative wood dust exposure and FEV_1, FVC or FEV_1/FVC.[242]

In another study of Zaman on rubber wood exposure and lung function among 87 workers in a plywood manufacturing company, a total of 12.6% of the workers had abnormal spirometry. Mean (range) inhalable dust exposure in personal sampling was 0.3 (0.06-0.85) mg/m^3. Multivariate analysis including age, height, smoking status, and estimated cumulative exposure to wood dust (working duration×measured exposure level) showed no significant correlation between wood dust exposure and FEV_1, FVC or FEV_1/FVC.[241]

Douwes et al. studied the association between dust exposure and lung function in 167 pine sawmilling workers with and 59 without asthma symptoms from five large sawmills in New Zealand processing exclusively pine. Full-shift (8 h) personal inhalable dust exposure was assessed (airflow 2 l/min) in 205 workers on the same day that lung function tests were carried out. Based on the GM±GSD dust concentration the workers were divided in three categories (non-/low/intermittent exposure (0.38±2.80 mg/m^3, n=92), high exposure to dry dust (0.62±2.23 mg/m^3, n=48), and high exposure to green dust (0.80±2.25 mg/m^3, n=43). The mean (±SD) dust concentration for all workers was 0.52±2.66 mg/m^3 (n=183). High exposure to dry dust was associated with asthma symptoms (adjusted OR 2.1, 95% CI 1.0-4.4), whereas no association with high green dust exposure (adjusted OR 1.4, 95% CI 0.6-3.3) was found. Subjects with asthma symptoms exhibited a significantly lower FEV_1 and PEF than those without asthma symptoms, whereas their FVC was very similar. High exposure to both dry and green dust were significantly associated with a reduction in FEV_1 and PEF. The FVC was also reduced in the high green dust exposure group. The exposure-related lung function deficits calculated separately for

subjects with and without asthma symptoms were only moderately different. The effect of cumulative or past exposures was not explored since no detailed information was available concerning past exposures and/or job titles.[48]

Bolund et al. 2017 studied the effects of organic dust exposure on long-term change in lung function with a meta-analysis. The meta-analysis included cotton, grain, paper, and wood workers as well as farmers (14 studies). Three studies concerning wood workers were included in the study. Overall, occupational organic dust exposure (cotton, grain, farm, paper, and wood dust) revealed an excess loss of FEV_1 by 4.92 ml/year (95% CI 0.14-9.69). No excess decline to FVC were found, annual decline was only 1.47 ml/year (95% CI -3.35–6.30). However, no subgroup analyses were performed.[17]

In conclusion, only three longitudinal studies examining the association of wood dust exposure and lung function were identified. The study of Noertjojo et al. showed a higher annual decline in FVC in sawmill workers exposed to Western red cedar total dust at >0.2 mg/m^3 in comparison to non-exposed controls, with an indication of dose-response.[153] This finding may be associated with Western red cedar's potential to cause asthma through sensitisation. The large study of Glindmeyer et al. did not show an association between estimated average wood dust exposure and lung function changes in workers exposed to hardwood and softwood dusts mean levels in the range of 0.77-2.5 mg/m^3 (inhalable dust) and 0.10-0.23 mg/m^3 (respirable dust), when excluding Western red cedar and other allergenic wood dusts.[67] Bolund et al. reported during the 6-year follow-up an excess of FEV_1 loss being equivalent to 125 ml among 38 females exposed to 3.75-4.71 mg/m^3-years to inhalable wood dust. In contrast, no such association was observed in men, where only smoking and asthma were linked to the decline in lung function.[18]

Holness et al. reported a significant cross-shift decline in FVC (-2.36% vs -0.15%, p=0.005) and in FEV_1 (-2.47% vs 0.15%, p=0.005) among wood-workers when compared to the controls, but no correlation between the level of wood dust exposure and observed lung function decline over the work shift. Woodworkers were exposed to (mean±SD) 1.83±1.51 mg/m^3 total dust, and to 0.29±0.31 mg/m^3 respirable dust.[88] Schlünssen et al. demon-strated a cross-shift change in FEV_1 among non-smoking woodworkers that was associated with estimated average exposure to wood dust.[189] However, a study of the same investigators concluded that that cross-shift change in lung function cannot be used to predict longitudinal changes in lung function among woodworkers exposed to relatively low levels of wood dust.97

There are also several cross-sectional studies focusing on lung function in woodworkers. A part of these studies indicate a negative association between estimated level of (total/inhalable) wood dust exposure and FEV_1,

FVC and/or FEV_1/FVC.[8,48,100,128,129,216,228,240] In other studies, a negative association is reported between estimated cumulative exposure and FVC, FEV_1, and/or FEV_1/FVC.[9,234] There are also studies where such associations have not been found.[7,16,19,241,242] The usefulness of these studies in assessing exposure-related long-term effects in lung function is hampered by their cross-sectional design. Variable statistical and exposure evaluation methods make the comparison of these studies challenging.

These seemingly inconsistent findings and the lack of a clear dose-response pattern may be partly explained by varying wood species and woodworking processes in the different studies, and also by varying exposure to other agents that might impair lung function (e.g., endotoxins). The results may also be impacted by a healthy worker selection bias. The wood dust related lung function decline indicated in the cross-shift study with the lack of a clear evidence on lung function decline in the longitudinal studies may indicate that asthma could be a more relevant endpoint for wood dust exposure than e.g., chronic obstructive pulmonary disease (COPD). Women might be more susceptible to lung function decline than men based on one good-quality study. Overall, knowledge about the effects of wood dust exposure on lung function in women is limited, because the number of women in most of the studies is low or zero.

10.2.4 Asthma

In a large registry-based study, all Finns employed in wood-processing industry in years 1985, 1990, or 1995 were followed for asthma incidence during the years 1986-1998. Incident cases included people with asthma reimbursed for medication by the national health insurance or registered as having occupational asthma. The risk of developing asthma was increased among woodworkers in comparison to office workers in the same industries, relative risk (RR) for men being 1.5 (95% CI 1.2-1.8; 1,189 cases) and for women 1.5 (95% CI 1.2-1.7; 286 cases). The asthma risk was also compared to estimated annual mean of wood dust exposure based on the job titles of the employees. Increased risk was observed in both genders for low (<0.5 mg/m^3 total dust) and medium (0.5-1.5 mg/m^3 total dust) exposure but not for the highest exposure category (≥1.5 mg/m^3 total dust). Healthy worker effect was proposed by the authors as one potential explanation of the absence of dose-response.[81] Cumulative exposures were not evaluated.

Pérez-Rios et al. published a meta-analysis on wood dust exposure and risk on asthma (clinically diagnosed or self-reported through interviews). Based on three cohort studies, 12 case-control studies and four mortality studies published 1991-2007, they estimated with a random effect model a pooled RR of 1.53 (95% CI 1.25-1.87) for asthma among workers occupationally exposed to wood dust. The RR among Caucasians was 1.59 (95% CI 1.26-2.00) and for Asian populations 1.15 (95% CI 0.92-1.44). When restricted to studies that adjusted for smoking, the RR was reduced to 1.19 (95% CI 1.02-

1.39).[166] This meta-analysis was not able to estimate dose-response gradients because in their 19 source studies such estimates were given in only two relatively weak studies. Generally, the criteria for inclusion of the studies were loose. Some of the included studies seem to be overlapping, especially six studies from Sweden, four by Torén et al.[222-225] and two by Flodin et al..[60,61] The studies by Flodin et al. do not report results for wood dust only but to any dust.

Zhang et al. published a meta-analysis on association of asthma (not further specified) and exposure to organic dusts. In this study exposures to wood and paper dust were combined. Based on 14 studies from 1994-2012 they got a summary OR of 1.62 (95% CI 1.38-1.90) for wood/paper dust and asthma.[243]

Schlünssen et al. studied the prevalence of lung function test verified asthma[186] using the sample of the same study population as described in Section 10.2..[187] A total of 302 woodworkers and 71 non-exposed subjects answered a respiratory health questionnaire, underwent a non-specific bronchial provocation test (histamine challenge) and skin prick tests with 12 common inhalant allergens. Of the participants, 74% were male. The overall GM exposure to inhalable dust was 0.96 mg/m^3. A tendency to increased asthma risk (defined as symptomatic bronchial hyperreactivity, BHR) was demonstrated among atopic woodworkers compared to atopic non-exposed subjects with OR 3.0 (95% CI 0.8-11.9). However, there were only 54 participants with asthma symptoms and BHR. Asthma was related to dust level, most pronounced for symptomatic BHR among atopics, with OR 22.9 (95% CI 1.0-523.6) for the highest inhalable dust level (>1.39 mg/m^3) compared with the lowest dust level (<0.80 mg/m^3). The OR (95% CI) for 0.80-0.99 mg/m^3 was 8.69 (0.47-159.82) and that for 1.0-1.39 mg/m^3 was 3.50 (0.19-64.96). The authors concluded that wood dust exposure was associated with asthma, despite a low dust level compared with other studies. Atopy was an important effect modifier in the association between asthma and wood dust exposure.[186]

Vested et al. studied the impact on hospital readmissions of wood industry workers for asthma in Denmark. They identified from the National Patient Registry all individuals with first diagnosis of asthma between 1997 and 2007 and who according to the data of the Supplementary Pension Fund registry had been blue-collar workers in wood industry after their initial asthma diagnosis. The 769 persons were followed for readmissions for asthma up to 31 December 2007 (mean follow-up time 3.9 years).
The exposure to wood dust was estimated with a quantitative industry exposure matrix (IEM) and adjusted rate ratios for wood dust exposure in the previous year was estimated with logistic regression. Asthma patients who were also exposed to farming dust (1.5%) were excluded. Exposure to wood dust increased the risk of hospital readmission for individuals with asthma. The rate ratio for exposure below the median level of persons exposed in the previous year (0.7 mg/m^3) was 2.38 (95% CI 1.23-4.60) and

for exposure above the median level 2.67 (95% CI 1.35-5.26) as compared to non-exposed.[229]

In conclusion, the meta-analyses of Pérez-Rios et al. and Zhang et al. indicate a 20-60% increase in asthma risk among workers occupationally exposed to wood dust, without providing further information on the dose-response.[166,243] The study of Vested et al. showed a twofold increase in the risk of hospital readmission in asthma patients occupationally exposed to wood dust, the risk being only slightly higher for persons with estimated mean exposure above 0.7 mg/m^3 than for those below 0.7 mg/m^3.[229] Atopy may be an effect modifier in the association between asthma and wood dust exposure.[186]

10.2.5 Chronic obstructive pulmonary disease

Shamssain et al. studied lung function of 145 non-smoking South African workers, who were exposed to pine wood or board fibre wood and 152 non-smoking controls without dust exposure, which were matched with age, height and weight. The mean total dust concentration in the factory was 3.82 (SD 1.34) mg/cm^3. The prevalence of FEV_1/FVC <0.7 was 30% among exposed workers and 17% among non-exposed workers (p<0.01). The prevalence was also significantly higher in the exposed workers with more years of employment.[194] Bolund et al. studied new-onset chronic obstructive pulmonary disease (COPD) and decline in a 6-year follow-up cohort of Danish furniture workers exposed to wood dust. A total of 927 men and 185 women participated in the baseline and follow-up appointments in 1997-1998 and 2003-2005, respectively. Exposure to inhalable dust was assessed as exposure level at baseline and as cumulative exposure in the follow-up period from quantitative task specific job exposure matrix and divided as low exposure (≤3.75 mg/m^3/year) and high exposure (3.75-7.55 mg/m^3/year. Only a trend for exposure-response relation was detected for new-onset COPD in highly exposed female smokers (OR 8.47, 95% CI 0.9-82.4, p=0.049). Among males only smoking was strongly associated to new-onset COPD.[18]

Vested et al. studied the impact on hospital readmissions of wood industry workers for COPD in Denmark. They identified from the National Patient Registry all individuals with first diagnosis of COPD between 1997 and 2007 and who according to the employment data of the Supplementary Pension Fund registry data had been blue-collar workers in wood industry after their initial COPD diagnosis. A total of 342 persons were followed for readmission for COPD up to 31 December 2007 (mean follow-up time 3.4 years). The exposure to wood dust was approximated with a quantitative industry exposure matrix (IEM) and rate ratios for wood dust exposure in the previous year was estimated with logistic regression. Exposure to wood dust did not increase the risk of hospital readmission for individuals with COPD. Four percent of the COPD patients which were also exposed to farming dust were excluded.[229]

10.2.6 Idiopathic pulmonary fibrosis

Idiopathic pulmonary fibrosis (IPF) is the most common distinct entity of the idiopathic interstitial pneumonias. Although the name suggests that there are no known causes of IPF, environmental agents are suggested to play a role in the aetiology.[144] Due to the rare nature of the disease the knowledge relies on the case-control studies.

Taskar and Coultas reviewed case-control studies of occupational and environmental risk factors for IPF from 1990. Their meta-analysis included five studies on wood dust exposure and risk of IPF. In these studies, the total number of wood dust exposed workers was 58 and non-exposed controls 625. According to the summary estimate, wood dust exposure was associated with increased risk of IPF (OR 1.94, 95% CI 1.34-2.81).[212] One of these case-control studies[90] showed an independent increase in the risk of IPF with wood dust exposure (OR 1.71, 95% CI 1.01-2.92) that was also associated with self-reported years of exposure ($p<0.001$), but the evaluation of the exposure level was lacking.[212]

Park et al. searched all studies until March 2020, but only the studies where IPF diagnosis was based on computer tomography, lung biopsy or autopsy findings were included. This systematic review and meta-analyses of included four case-control studies (1,599 subjects) investigating wood dust exposure. Based on these studies, exposure to wood dust was associated with an increased risk of IPF (OR 1.62, 95% CI 1.04-2.53). Additionally, in four studies (1,631 subjects) exposure through working in the wood working industry was analysed. This factor tended to increase IPF risk with OR 1.56 (95% CI 0.87-2.82).[162] Quantitative analysis considering the degree and frequency of exposure were lacking in the included studies.

Pauchet et al. included in their review and meta-analysis all original articles published in English or French up until August 2021. There were ten case-control studies investigating wood dust exposure, but only three of them specially considered the type of wood which patients were occupationally exposed. Based on these studies, exposure to general wood dust was associated with the pooled estimated increased risk of IPF (OR 1.32, 95% CI 1.02-1.71). Noteworthy, only seven studies provided adjusted results on smoking and demonstrated the pooled OR for IPF to be only 1.16 (95% CI 0.83-1.61). Based on three studies the risk was higher for hardwood exposure (OR 1.75, 95% CI 1.13-2.70) compared to softwood exposure (OR 1.4, 95% CI 0.9-2.16). Adjustment for smoking was done in only one study, in which exposure to hardwood dust was not associated with an increased risk of IPF (OR 0.51, 95% CI 0.17-1.58).[164]

In conclusion, based on three meta-analysis of case-control studies an association between wood dust exposure and IPF is possible, but the significance of risks is probably modified by tobacco consumption. The risk of IPF may be higher in woodworkers exposed to hardwood. The three meta-analyses included several overlapping studies. The knowledge about

dose-responses between the levels of wood dust exposure and development of IPF is lacking.

10.3 Genotoxic effects and biomarkers of reactive oxygen species

DNA damage was assessed by the comet assay in peripheral blood leukocytes from 35 wooden furniture manufacture workers (21 females and 14 males, mean age 40±8) and from 41 unexposed controls (32 females and 9 males, mean age 43±8). More cells with DNA damage (21.5%) were observed in the woodworkers than in the control persons (9.7%), and statistically significant differences in the frequency of damaged cells were detected between exposed and controls both before and after DNA repair ($p<0.005$). Cigarette smoking significantly increased the percentage of damaged cells among the control persons but not among the exposed workers.[161] Exposure levels of wood dusts or other compounds in the furniture manufacture were not studied or reported.

Frequency of micronuclei and other nuclear alterations was studied in buccal epithelium samples of 20 male furniture workers (10 smokers and 10 non-smokers) exposed to a mixture of soft and hardwood dust, and 20 healthy male controls (10 smokers and 10 non-smokers). Dust levels in the workplace, estimated based on dust accumulated on surfaces during a single workday, were between 4.7-28.9 mg/m^3. Micronucleus frequency in exfoliated buccal mucosal cells (mean±SD) was 6.63±1.65% in the workers and 1.50±1.18% in controls. Evidence of nuclear injury (karyolysis, karyorrhexis) and number of binucleated cells was also increased in the furniture workers. Smoking significantly increased the frequencies of micronuclei and other nuclear changes in both controls and exposed subjects. In the non-smoking workers the micronucleus frequency (mean±SD) and level of other nuclear injury were higher than in the non-smoking controls (e.g., micronucleus frequency 5.50±1.07% in the workers and 0.90±0.58% in controls), but statistical significance was not reported for these groups separately from the smokers.[26] Study did not include evaluation of the dust particle size range, and no dust measurements were performed for the control subjects.

Markers of genotoxicity were studied using peripheral blood lymphocytes and buccal epithelial cells collected from 60 male furniture workers (30 smokers and 30 non-smokers) occupationally exposed for more than 5 years to a mixture of softwood (guava, deodar, Pinus and Picea species) and hardwood (teak, ash, mango, neem, tamarind, sandal wood, rose wood and satin wood) dusts in comparison to 60 healthy male controls (24 smokers and 36 non-smokers). Exposure levels (7.4-25.8 mg/m^3) were estimated based on the amount of wood dust accumulated on the surface of work area during a workday. Comet assay in leukocytes showed significantly increased levels of DNA damage (mean comet tail length±SD in µm) in wood dust exposed workers (14.35±2.47 µm) compared to the controls (7.08±2.21 µm) ($p<0.05$). The frequency of micronuclei (mean±SD)

in buccal cells was higher in wood dust exposed workers (2.83±1.16%) than in controls (0.40±0.13%) ($p<0.05$). Increased frequencies of micronuclei (mean±SD) (5.08±0.99% in workers vs. 3.15±0.87% in controls, $p<0.05$) and chromosomal aberrations (mean±SD) (7.98±1.06% in workers vs. 3.15±0.82% in controls, $p<0.05$) were also detected in the peripheral blood lymphocytes of workers. Activity of antioxidant enzymes, superoxide dismutase and glutathione peroxidase, but not catalase, was reduced in the workers. Age, smoking, alcohol consumption and duration of wood dust exposure per day had a significant effect on the studied endpoints but non-smoking workers had significantly higher frequency of MN in buccal cells and in lymphocytes as well as CA compared to the non-smoking controls ($p<0.05$).[175] Dust particle size range or exposure levels of control subjects were not studied or reported.

Genotoxic effects were examined in the nasal and buccal cells of 31 male workers exposed to wood dust (fir, spruce, beech, oak, and wooden boards such as MDF and wood melamine) compared to 19 non-exposed controls. All study participants were non-smokers or ex-smokers for a minimum of one year. Inhalable dust was determined with personal air samplers (flow rate 2 l/min) for two 8-hour working shifts. The geometric mean±GSD dust concentrations were 2.9±2.5 mg/m^3. The MN frequency (mean±SD) in nasal cells was significantly higher in the exposed group (3.2±2.2%) compared to non-exposed controls (0.9±0.8%) ($p<0.001$). Buccal cell MN frequency (mean±SD) was higher in the exposed workers (2.8±1.5%) compared to the controls (1.6±0.8%) ($p<0.001$). Micronucleus frequencies increased with the duration of wood dust exposure (in nasal cells OR 1.6 per decade of exposure, in buccal cells OR 1.2 per decade of exposure), but no dose-response between wood dust exposure per day and micronucleus frequency was found.[21]

Micronuclei and other indicators of genetic damage were investigated in buccal and nasal cells from 51 workers of a veneer factory (25 males, 26 females) exposed to volatile wood-derived compounds, 38 carpenters of a furniture factory (35 males, 3 females) which used no synthetic chemicals and 65 control subjects matched for sex, age, body mass index (BMI), smoking and alcohol consumption. Veneer factory workers were exposed to wood dust and additionally to volatile organic compounds (VOC) which are released during the cooking process. The veneer was made from both softwood (55%) and hardwood (45%) dust. The softwood species used were stone pines (20%), spruce (19.5%), larch (13%), acacia (0.94%) and yews (0.02%). The hardwood fraction consisted of oak (30%), maple (6.5%), beech (6.5%), the rest were apple and pear, chestnut and cherry. Furniture factory workers used different woods without synthetic chemicals or formaldehyde. These subjects were solely exposed to wood dust and organic glue. They worked with 94% press boards made solely of spruce wood, 6% of the boards which consist of 60% spruce, 20% oak and 20% beech wood. The levels of inhalable wood dust were measured with personal air samplers (air flow 3.5 l/min) and stationary samplers (air flow 10

l/min) for 8 hours. The level of inhalable dust was 0.39 mg/m^3 in the veneer factory and 0.66 mg/m^3 in the furniture factory. In nasal cells no statistically significant differences in the frequency of micronuclei were detected between exposed workers and non-exposed controls, but the rates of other nuclear anomalies (nuclear buds, karyorrhectic and karyolitic cells) were significantly increased by wood dust exposure. In buccal cells frequency of micronuclei was higher in exposed workers compared to controls ($p<0.05$) and significant differences were also detected in the frequency of other nuclear anomalies. Duration of exposure or background factors (gender, age, smoking, alcohol consumption and BMI) were not associated with the detected frequency of micronuclei or other nuclear anomalies.[238]

In the same study population as in Bruschweiler et al.,[21] elevated levels of DNA damage, assessed by the comet assay, were identified in the workers exposed to dust from composite wood products such as plywood, particle board, fibreboard and MDF compared to non-exposed controls ($p<0.001$). Comet score in 100 cells was 11.3 (25th-75th quartile 8.8-26.3) in workers exposed to natural wood, 61.5 (25th-75th quartile 49.5-85) in workers exposed to wooden board and 11.0 (25th-75th quartile 8.0-18.0) in the non-exposed control group (11.0).[22] The study indicates that composite wood products contain or produce, during power tool manipulations, substances (e.g., formaldehyde, isocyanate, or epichlorohydrine) leading to acute DNA damage, but concentrations of these chemicals were not determined in the study.

Association between wood dust and oxidative DNA damage (M_1dG adducts in nasal epithelium and urinary 15-F_{2t}-isoprostane) was studied in 136 male woodworkers (50 smokers, 25 ex-smokers) and in 87 matched controls (26 smokers, 11 ex-smokers). The mean daily concentration of airborne wood dust, as quantified by an 8-hour TWA, was 1.48 mg/m^3. The frequency of M_1dG was significantly higher (up to 1.7-fold) among the workers exposed to wood dust as compared to the controls. The overall mean ratio between the exposed workers and controls was 1.28 (95% CI 1.03-1.58). A linear correlation was found between M_1dG adducts and the urinary excretion of 15-F_{2t}-isoprostane supporting the role of oxidative stress in wood dust genotoxicity. M_1dG levels were also significantly correlated to occupational history (mean ratio 2.47, 95% CI 1.67-3.62). Current smokers had higher level of M_1dG than ex-smokers or non-smokers, but the difference was not statistically significant.[27]

Biomarkers of oxidative stress (15-F_{2t}-isoprostane and 8-oxo-dGuo) were studied in 127 woodworkers (48 smokers, 79 non-smokers) operating in different sectors of the wood industry and 111 unexposed controls (28 smokers, 83 non-smokers). Tobacco smoking was assessed by measuring cotinine in urine. The inhalable fraction of dust was measured using personal samplers (air flow 4 l/min) for 8 hours. Median value of wood

dust concentration near the breathing zone of exposed workers was 0.34 mg/m^3. Levels of 15-F_{2t}-isoprostane were higher in exposed workers (3.29 ng/mg creatinine) as compared to the controls (2.51 ng/mg creatinine) (p=0.004). No statistically significant differences were reported for 8-oxo-dGuo. Both studied biomarkers of oxidative stress were significantly correlated with exposure to wood dust (p=0.01 for 15-F_{2t}- isoprostane, p=0.004 for 8-oxo-dGuo) and cotinine (p=0.05 for 15-F_{2t}-IsoP and p=0.001 for 8-oxo-dGuo). Multilinear regression analysis, adjusted for cotinine, exposure to wood dust, ventilation, formaldehyde, residence and age, showed that 15-F_{2t}-IsoP level was positively and significantly influenced by cotinine and formaldehyde, and 8-oxo-dGuo level was influenced cotinine, formaldehyde and exposure to wood dust.[65] The data was not presented separately for smokers and non-smokers, but effect of tobacco use was explored by measuring cotinine levels and with multilinear regression model.

In addition, one study explored genotoxic effects of fumes emitted from heated wood. Peripheral blood lymphocytes of 13 non-smoking male plywood factory workers (mean age 47 years) and 15 non-smoking age-matched male controls, were studied for chromosomal aberrations. The frequency of chromatid breaks was 2.1% in the workers exposed to fumes and 1.0% in the controls (p~0.01). It was concluded that the emissions from wood itself, consisting mostly of monoterpenes, were the most likely cause of the observed genotoxicity. Exposure levels of wood dusts or other compounds in the plywood factories were not studied.[113]

In conclusion, in the reviewed studies wood dust exposure was shown to induce genotoxic changes locally in the buccal and nasal epithelium. Induction of systemic genotoxicity, DNA and chromosomal damage, in blood lymphocytes was also reported as well as increased levels of biomarkers of oxidative stress. The data do not allow distinction between softwood and hardwood exposures. Studies typically compared exposed and non-exposed workers, and dose-response relationships were not investigated. The lowest exposure level of inhalable wood dust, 0.39 mg/m^3, resulting in increased levels of buccal micronuclei was reported by Wultsch et al.,[238] without induction of micronuclei in the nasal cells. Bruschweiler et al. reported elevated levels of both buccal and nasal micronuclei at 2.9±2.5 mg/m^3 of inhalable wood dust.[21] Increased levels of biomarkers of oxidative stress and oxidative DNA damage were detected at exposure levels of 1.48 mg/m^3 and 0.34 mg/m^3.[27,65] Some studies point out that in addition to wood dust, exposure to other chemical substances in the workplace could have influenced the recorded genotoxicity.
As smoking is a strong risk factor for nasal, nasopharyngeal and lung cancers, cigarette smoking among the study subjects may limit the accurate assessment of the effects of wood dust exposure. Smoking status of the participants was reported to be a confounding factor in many of the studies.

10.4 Carcinogenic effects

Siew et al. 2012 studied the effect of wood dust and formaldehyde exposure to risk of **nasal, nasopharyngeal and lung cancers** among all 1.2 million Finnish men born 1906-1945 who participated in the 1970 census. Cancer cases diagnosed 1971-1995 were identified from the Finnish Cancer Registry. Average cumulative exposures of wood dust (inhalable airborne dusts of any tree species, in Finland mainly softwood) and formaldehyde in each 5-year calendar period, 5-year age stratum and each occupation were estimated using the occupation recorded in the 1970 census and the Finnish job exposure matrix (FINJEM) and assuming that the person had been working in the same occupation from age 20 until observation period minus 20 years lag. Aggregate level estimates of potential confounding factors (occupational exposure to silica dust and asbestos, smoking prevalence) were done in a similar way. In the multivariate statistical analysis, smoking and exposure to silica dust and asbestos showed an excess risk of **lung cancer** (30,137 cases) but exposure to wood dust showed no excess risk. There was no association between wood dust and **nasopharyngeal cancer** but the numbers of cases (only 7 cases in the wood dust exposed occupations) makes this finding uninformative. For **nasal cancer**, there was a statistically significant excess (RR 1.59, 95% CI 1.06-2.38) based on 32 cases in wood dust exposed and 260 cases in unexposed occupations. There was no increase in risk with increasing cumulative exposure. The RRs were slightly higher for nasal cancers histologically confirmed as squamous cell carcinomas (57% of all cases).[196] The RR estimates in this study were probably diluted towards 1.0 due to exposure misclassification, i.e. that study participants were incorrectly categorized with respect to their true exposure.

In a later study by Siew et al. 2017 on the effect of wood dust to risk of **nasal and nasopharyngeal cancer** the methodology was similar to that in Siew et al. 2012.[196] with three essential improvements: the data were extended with data from Sweden, Norway and Iceland; the observation period was extended to 1961-2005; and the occupational histories from several censuses were available and made it possible to estimate the duration of working in wood dust exposed occupations for each study subject. The wood types used in the Nordic countries include both softwoods (mainly domestic) and hardwood (mainly imported). The study was restricted to men only. There were 393 cases of nasal adenocarcinoma, 2,446 cases of other types of nasal cancer and 1,747 cases of nasopharyngeal cancer. These numbers are much higher than in other studies related to these rare cancer types and hence the importance of the findings of this study is high. Five population controls were selected for each case, matched by year of birth and country. Cumulative exposure (CE) to wood dust (and to formaldehyde as a potential confounder) for each case and control was estimated by multiplying the probability and level of exposure in each occupation (taken from a job exposure matrix created for Nordic countries) with the duration of the person having worked in each occupation. The changes in exposure levels through decades were taken

into account by using period-specific exposure estimates. The analyses revealed a very strong association between wood dust and **nasal adenocarcinoma**. The hazard ratio (HR) for the lowest exposure category (CE below the median of all exposed study subjects; ≤6.70 mg/m^3-years) was 3.16 (95% CI 2.08-4.81) and increased to 28.9 (95% CI 9.81-84.9) in the highest exposure category (highest decile of the CE; ≥28.82 mg/m^3-years). Adjustment for formaldehyde exposure decreased the HRs to 3.11 (95% CI 2.04-4.75) and 16.5 (95% CI 5.05-54.1), respectively. In both analyses, a dose-response effect was evident (p-trend<0.0001). For nasal **cancer other than adenocarcinoma**, and for **nasopharyngeal cancer** there was no significant excess and no dose-response association.[197] The risk estimates in this study are probably diluted towards 1.0 but not as much as in Siew et al. 2012[196] because of access to individual level estimates of duration of the exposures.

Demers et al. 1995 summarised in a pooled reanalysis findings on the association between wood dust exposure and **sinonasal cancer** from 12 case-control studies from seven countries published 1982-1993.
The combined data set included 930 cancer cases, out of which 195 were classified as adenocarcinoma. In men, the OR for **nasal adenocarcinoma** was very high (OR 45.5, 95% CI 28.3-72.9) in jobs with highest wood dust exposure. The numbers of exposed cases among the women were essentially smaller and the findings were weaker. There was no indication of an excess risk of nasal cancer other than adenocarcinoma among persons exposed to wood dust.[44] These results were dominated by the French data with the largest number of cases and the highest ORs for adenocarcinoma.

The systematic review and meta-analysis by Alonso-Sardón et al. 2015 described 70 studies on wood dust and various types of cancers but only gives a meta-estimate for **nasal adenocarcinoma**. The meta-OR was 10.3 (95% CI 5.9-17.9) (6). Much of the evidence comes from the data of wood-workers in the Nordic countries,[170] i.e., based on the same cases as the dose-response analysis results by Siew et al. 2017.[197]

Another review and meta-analysis on occupational risk factors on sinonasal cancer published in 2015 is the one by Binazzi et al. This paper describes 63 studies but only uses 3 cohort studies and 11 case-control studies in the meta-analysis on wood dust exposure. The pooled RR for **nasal adenocarcinoma** was 35.3 (95% CI 20.6-60.3) in the cohort studies and 29.4 (95% CI 16.5-52.6) in the case-control studies. The meta-RR for **nasal squamous cell carcinoma** was 1.41 (95% CI 1.01-2.10).[14] The cohort study by Siew et al. 2012[196] described above was used as one element of the meta-RRs.

Pesch et al. 2008 conducted a case-control study on wood dust and risk of **nasal adenocarcinoma**. The cases were men with nasal adenocarcinoma recorded as recognised occupational disease by an insurance association of wood workers 1995-2003. Out of 129 eligible cases, 57 men and 29

next-of-kin (67%) participated. The controls were men recruited from the same data base who had had accidents on their way to/from work or during the work shift. The final number of controls was 204 (response rate 75%). The OR for the highest category of cumulative wood dust exposure (≥200 mg/m^3-years) as compared to the lowest cumulative exposure category (<140 mg/m^3-years) was 4.20 (95% CI 1.69-10.4). The OR for the highest category of average wood dust exposure (≥5 mg/m^3) as compared to the lowest category (<3.5 mg/m^3) was 48.5 (95% CI 13.3-176). Pesch et al. concluded that the excess risk in their data is probably more related to hardwood than softwood.[167]

d'Errico et al. 2009 conducted a case-control study on Italian patients hospitalised between 1996-2000 for sinonasal epithelial cancer (113 cases, 336 hospital controls), and found a significantly increased risk of **nasal adenocarcinoma** among persons ever-exposed to wood dust (OR 58.6, 95% CI 23.7-114.8). Also, an increased risk of sinonasal cancer histotypes other than adenocarcinoma and squamous cell carcinoma was observed among ever-exposed (OR 5.5, 95% CI 1.99-15.24). Cumulative exposure to wood dust and other agents, including solvent vapours, formaldehyde, PAHs, arsenic, and chromium and nickel compounds, was evaluated semi-quantitatively based on working history information, by weighting the working years in each task with the estimated probability and intensity of the exposure. There was a significant increase in the risk of sinonasal adenocarcinoma with increasing estimated cumulative exposure (weighted years of exposure) of wood dust (p<0.0001). The regression model applied adjusted for age, sex, smoking and co-exposures, and allowed for a 10-year latency period.[39]

Soćko 2021 in her mathematical modelling utilised the exposure category specific risk estimates by d'Errico et al..[39] Based on these data, Soćko built continuous linear, quadratic and exponential model functions.
The exponential model turned out to be best suited to the empirical data and became the basis for estimating the risk of sinonasal cancer for cumulative exposure (weighted years of exposure) of wood dust. According to this model, the estimated OR of developing **nasal adenocarcinoma** after 35 years of >1 mg/m^3 exposure (or longer duration of lower-intensity exposure) to wood dust was approximately 300 (95% CI ~50-1,200), and of developing **other types of sinonasal cancer** approximately 18 (95% CI ~5-80), in comparison with non-exposed persons.[202] Although the modelling was based on a quite small data set and the only measure of wood dust exposure was the weighted duration in wood-exposed work, this model seems to fit quite well with the other estimates of wood dust exposure and sinonasal cancer.

Leivo et al. 2021 determined the proportions of ITAC and non-intestinal-type **adenocarcinoma** in 56 sinonasal adenocarcinoma patients in France and Finland and related them with wood dust exposure histories. Non-intestinal adenocarcinomas were more common than ITAC in Finland

(12 vs 9 cases), while in the French samples there were 6 non-intestinal vs 29 ITAC cases). The authors suggested that such a remarkably dissimilar occurrence of these tumours may reflect different pathogenetic circumstances in the two countries, and also perhaps different patterns of wood dust exposure (in Finland mainly softwoods and in France mainly hardwoods).[118] This is the only comparison of the occurrence of ITAC and non-intestinal-type adenocarcinoma between countries with different wood usage but gives a hint that ITAC might be more strongly associated with hardwood dust than the non-intestinal type.

Acheson et al. 1984 studied causes of death among 5,108 men who had been working in furniture factories in Buckinghamshire in England any period before 1969 and known to be exposed to hardwood dust. The object was to resolve whether the well-known risk of **nasal adenocarcinoma** was also associated with an increased mortality. The standardised mortality ratio (SMR) for nasal cancer was 8.1 (95% CI 3.7-15.5, 9 deaths). The SMR in the dustiest occupations was 15.8 and increased with increasing work duration. All nine nasal cancers were adenocarcinomas, and it was estimated that the risk for dying from nasal adenocarcinoma in the study population was at least 80-fold as compared to the general male population in Buckinghamshire.[3]

Vaughan et al. 2000 studied the association between wood dust and **nasopharyngeal cancer** in the US. The cases were identified from 5 registries of The Surveillance, Epidemiology, and End Results Program (SEER) 1987-93 and controls selected from the general population through random digit dialling. Information on occupational histories and other factors potentially related to nasopharyngeal cancer risk were collected via structured telephone interviews. In 19% of cases and 1% of controls the interviewed persons were spouses of other proxy persons. In the final data, there were 17 cases ever exposed to wood dust and 125 unexposed ones. ORs were calculated for both maximum exposure and cumulative exposure. For both of these measures, the middle exposure category showed an OR clearly >1.0 while the highest category showed an OR clearly <1.0. None of the ORs were statistically significant.[227] In addition to the low power, this study suffered from selection and recall biases and therefore has little value in evaluation the effect of wood dust exposure to risk of nasopharyngeal cancer.

Ekpanyaskul et al. 2015 studied the association between wood dust exposure and **nasopharyngeal cancer** in a case-control study in Thailand.[52] They re-used data collected for the Thai nasopharyngeal cancer risk factor project[51] with 327 newly diagnosed cases and 327 controls (visitors of the same hospitals) matched by gender and age were interviewed. The wood dust exposure was assessed from the occupational history information by three experts who did not know the case-control status of the subjects. Almost all cases (97%) were non-keratinizing carcinomas. For this type, there was an association with duration and cumulative exposure of wood

dust, with ORs of 2.26 (95% CI 1.10-4.63) and 2.17 (95% CI 1.03-4.58) among those exposed for ≥10 years and having more than median cumulative exposure, respectively.[52] The number of keratinising nasopharyngeal carcinoma cases, which is the predominant type in low-incidence countries, was so small that ORs for this type of nasopharyngeal cancer were not given separately. The data shown in the paper however, give indirect information suggesting that there was no excess risk related to wood dust exposure.

The meta-analysis by Beigzadeh et al. 2019 included 7 case-control studies on wood dust and **nasopharyngeal cancer**.[11] Three of them (referred above[52,197,227]) made up 60% of the weight of the meta-OR of 1.50 (95% CI 1.09-2.07) for being occupationally exposed to wood dust. The meta-estimate was elevated due to elevated ORs in the four Asian studies with ORs varying from 1.61 to 4.10.[11]

A parallel meta-analysis on wood dust and **nasopharyngeal cancer** was made by Meng et al. 2020.138 They included six out of the seven studies also included by Beigzadeh et al. 2019,[11] and added 4 other case-control studies (3 from Asia, 1 from New Zealand) and a pooled reanalysis on cancer mortality in five Nordic cohorts of workers in wood-related industries.[43] The pooled OR was 2.18 (95% CI 1.62-2.93). In these meta-analyses, the explanation for finding high ORs in Asia but not in the Nordic countries is thought to be related to genetics and occupational safety practices. Another explanation might be the high proportion of non-keratinising nasopharyngeal carcinoma in Asian countries, which seems to be more associated with hardwood dust exposure than the keratinising type.

The French study by Laforest et al. 2000 assessed the risk of **hypo-pharyngeal** and **laryngeal cancers** related to wood dust exposure.
The cases were male patients with laryngeal or hypopharyngeal squamous cell carcinoma identified from 15 French hospitals in 1989-1991. Out of the 664 eligible cases, 21% could not be interviewed and some others were excluded because they did not answer to questions on alcohol use or did not use alcohol at all – these few men were assumed to be mainly former drinkers who had stopped for health reasons – leaving in the final analysis 296 men with laryngeal cancer and 201 men with hypopharyngeal cancer. Altogether 296 controls were selected among patients treated for other cancers in hospitals nearby. This study observed an OR of 1.52 (95% CI 0.59-3.94) for hypopharyngeal cancer in the highest category of cumulative exposure of wood dust while other ORs were close to 1.0 and none of the ORs was statistically significant.[114] In addition to the low power, this study suffered from selection and recall biases and therefore has little value in evaluation the effect of wood dust exposure to risk of laryngeal cancer and hypopharyngeal cancers. A further weakness is the use of controls with cancer diagnoses which may be linked to the same risk factors as the cases.

The meta-analysis by Paget-Bailly et al. 2012 gives relative estimates on effect size on risk of **laryngeal cancer** among wood workers based on 18 case-control studies and 4 cohort studies published 1986-2008.
The overall effects size for the lowest wood dust exposure category reported in the papers was 0.95 (95% CI 0.81-1.12) and for the highest category 0.95 (95% CI 0.80-1.14).[159]

Meng et al. 2024[137] carried out a meta-analysis using the same 18 case-control studies and one of the four cohort studies as used by Paget-Bailly et al. 2012,[159] along with one more recent cohort study published in 2013 by Langevin et al..[115] The meta-analysis by Meng et al.[137] contains several major methodological shortcomings with regards to analyses (see Smit 2025).[201]

A case-control study conducted in Serbia and Montenegro observed an increased risk of cancer of the **oropharynx** (OR 2.33, 95% CI 0.96-5.66) associated with wood dust (self-reported, ever-exposed). The study consisted of 100 cases of oropharyngeal cancer (89 men and 11 women) diagnosed consecutively during 1998-2000 and 100 controls treated during the same period for non-cancerous diseases of the head and neck (most frequently nasopharyngitis, sinusitis, rhinitis and pharyngitis) matched for age, sex and place of residence. The ORs were adjusted for education, BMI, smoking, alcohol, and family history of oropharyngeal cancer.[232] The level of exposure was not evaluated. All controls were patients sampled from the same institution as the cases and treated for non-cancerous head and neck diseases, which could also be associated with wood dust exposure.

A Finnish case-control nested in a cohort of male woodworkers studied the effect of wood dust exposure and several chemical exposures to risk of **respiratory cancers**. The wood dust exposures in this cohort were rather low and mainly from softwood species. Among the 7,307 workers from 35 plants there were 136 cases of respiratory cancer diagnosed 1957-1982. For each cancer case, three controls were selected from the same cohort, matched by year of birth. The only suggestion of an association was the OR of 1.09 (95% CI 0.60-1.99) for all respiratory cancers combined in the highest cumulative wood dust exposure category (>5 mg/m^3-years), in a model adjusted for smoking and with a minimum induction period of 10 years.[104] Although this finding is in a stratum which could indicate a causal association, it is weak and based on 27 exposed cases only. In the results given for upper tract respiratory cancers and lung cancer separately there is no indication of an association. The size of the study is limited but still essentially larger than in the articles published from the partially same data.[101,105] This new study[104] is also essentially better than the two earlier studies in terms of data quality and statistical analysis methods.

Bhatti et al. 2011 studied the association between wood dust and **lung cancer** in the US state of Washington. The cases were identified from one of the SEER registries 1993-1996 and the controls were selected from the

general population through random digit dialling. Information on occupational and hobby-related wood dust exposures and other factors potentially related to lung cancer risk were collected via telephone interviews. Subjects requiring proxy respondents were excluded. The final study data included 440 cases and 845 controls. All analyses were adjusted for smoking (never, former, current). There was no excess risk of lung cancer nor of any histological subtype of lung cancer in any of the categories of cumulative exposure to wood dust.[13]

The meta-analysis by Hancock et al. 2015 is based on 85 publications on **lung cancer** and wood dust exposure written in English (n=82) or Chinese (n=3). The paper reports numerous meta-estimates stratified by method of exposure estimation and other factors but no results on dose-response relations. In 23 studies, it was possible to adjust for smoking. These studies showed a RR (95% CI) of 1.31 (1.10-1.56), i.e., slightly higher than the estimate based on all 85 studies (RR 1.25, 95% CI 1.11-1.41). The studies from the Nordic countries – with predominantly soft-wood exposure – suggest a decreased risk of lung cancer among wood dust exposed persons (RR 0.63, 95% CI 0.30-0.99) - while in the studies made elsewhere the RR was 1.34 (95% CI 1.19-1.50).[74] The findings by Kauppinen et al. 1993[104] and Siew et al. 2012[196] described above are included in the meta-estimates and have a large effect in the estimate for the Nordic countries.

Curiel-García et al. in their systematic review and meta-analysis of the scientific literature summarised the risks of wood dust-related occupations on development of small cell lung cancer (SCLC). They included in their analyses eleven studies with a total of 2,368 SCLC cases and 357,179 controls. Exposure to wood dust at any time carried a significantly higher risk of SCLC (RR 1.41, 95% CI 1.11-1.80) as compared to non-exposed, with quite similar results in the studies. When the two studies which did not include adjustment for smoking were dropped, the RR decreased to 1.27 (95% CI 0.95-1.70).[38]

To conclude, it is evident from the data presented above that there is a strong relationship between cumulative exposure to wood dust and nasal adenocarcinoma with very high ORs or RRs for both hardwood dust and softwood dust. The data do not allow estimation of RRs for specific species of trees. The risk seems to increase in a supra-linear manner starting from quite low exposure levels, and the data do not allow for identification of an effect threshold. There may also be a weak relationship between cumulative wood dust exposure and non-adenocarcinoma sinonasal cancer but there are not many studies that have focused on other histologically confirmed types than adenocarcinoma. It seems that there is an association between the risk of nasopharyngeal cancer and wood dust exposure in Asian study populations where non-keratinising carcinoma is the dominating type but not in Nordic populations where non-keratinising carcinoma is rare.

The findings for oropharynx, hypopharynx, larynx and lung do not allow conclusion on an association with wood dust.

10.5 Reproductive and developmental effects

A registry-based case-control study in Sweden, Finland and Norway assessed the association between parental prenatal exposures in wood-related jobs and risk of testicular germ cell tumours (TGCT) in offspring.[36] The study was based on the idea that exposure to wood dust may induce oxidative stress in testicular tissue and germ cells which may then impact the cancer risk. The study included 8,112 TGCT cases diagnosed at ages 14-49 years between 1978 and 2012 with no history of prior cancer, and 26,264 controls matched by year and country of birth. Parents of cases and controls were identified via linkages with the population registries and their occupational information was retrieved from censuses. The job exposure matrix of the Nordic Occupational Cancer (NOCCA) project was used to assign occupational exposures to each parent. Maternal wood-related job was not associated with the risk of TGCT in offspring (OR 1.08, 95% CI 0.55-2.14), while paternal wood-related job was associated with a decreased risk of TGCT in offspring (OR 0.85, 95% CI 0.75-0.96). None of the specific wood-related jobs, such as upholsterers, sawyers, or construction carpenters, were significantly associated with a risk of TGCT. The only exception was an increased risk in the small group of sons of fathers working as ‘cabinetmakers and joiners’ the year before conception (OR 2.06, 95% CI 1.00-4.25). This large-scale analysis provided no evidence of an association between parental prenatal exposures in wood-related jobs and TGCT in sons.[36]

Rossides et al. compared the parental occupational dust exposure between children diagnosed with cancer from 1960 to 2015 and matched population controls. Exposures were assessed using a Swedish modification of FINJEM and occupational information from censuses 1960-1990 and other registry data. There were 9,653 children diagnosed with a childhood cancer and 172,194 controls who had an employed mother for whom it was possible to estimate occupational exposure. The respective numbers for analyses of paternal exposure were 12,521 and 274,434. Maternal wood dust exposure was associated with an increased risk of non-Hodgkin lymphoma (OR 2.03; 95% CI 1.21-3.40; 18 cases). The respective OR for paternal wood dust exposure was 0.84 (95% CI 0.51-1.38; 18 cases). Other types of childhood cancers did not show any association with parental wood dust exposure.[181] This is the only study so far to suggest a link between maternal occupational exposure to wood dust around pregnancy and non-Hodgkin lymphoma in the offspring and should be interpreted with caution.

11 Dose-effect and dose-response relationships

11.1 Nasal, eye and respiratory symptoms

The studies on woodworkers have reported wood dust to cause several different symptoms on nasal, eye and respiratory system compared to non-exposed controls, using mainly questionnaire data. The most relevant data on wood dust irritation effects is based on cross-sectional studies. The wood species, woodworking methods, exposure measurement methods, as well as the size of study populations, vary widely between the studies. Also, the potential dose-response relations are poorly addressed in most of the studies described in Section 10.2.

The variety of upper airway symptoms reported in the studies were nasal congestion, blocked nose, runny nose, nasal irritation, sneezing, and sore throat. Workers exposed to inhalable wood dust levels of 0.74-1.42 mg/m^3 or higher had a significant increase in nasal congestion during the work shift, compared to before work. In addition, positive correlation was observed between concentration of dust and change in mucosal swelling.[185]

Cough, wheezing, chest tightness, phlegm, dyspnoea, and irritation were reported in the studies as lower airway symptoms (Table 13). Inhalable wood dust exposure at >0.74-1.42 mg/m^3 was associated with wheeze, night wheeze, and daily coughing, in comparison to exposure at ≤0.74 mg/m^3. Exposure at >1.42 mg/m^3 was significantly associated with chest tightness, night wheeze, and daily coughing. Also, exposure to ≥1 mg/m^3 of inhalable wood dust was related to increased morning cough, daily coughing, and throat symptoms compared to controls never exposed to wood dust. Workers exposed to wood dust levels below 1 mg/m^3 only had an increased risk of morning cough.[187]

The reported eye symptoms included irritation, itching, redness and watering of eyes. Sawmill workers exposed to Western red cedar total dust at ≥2 mg/m^3 reported significantly more frequently eye irritation symptoms (31%) compared to workers exposed to <2 mg/m^3 (total dust) (5-8%).[228]

The overall prevalence of itchy skin/skin rash symptoms in exposed group was 1.1% vs. 0.2% in non-exposed group (adjusted OR 6.3, 95% CI 0.8-52.2) at GM inhalable wood dust level of 3.9 mg/m^3.[178]

In conclusion, there seems to be an increase in the self-reported nasal, eye and respiratory symptoms after inhalable wood dust exposure at around 1 mg/m^3 (Table 13). However, detailed information on the dose-response relationship for the variety of these symptoms is not available (Table 14).

11.2 Lung function changes

The most relevant data about wood dust exposure related lung function decline is based on three longitudinal studies. First, Noertjojo et al. studied Western red cedar exposed sawmill workers without reported doctor-diagnosed asthma in an 11-year follow-up. Western red cedar is known to cause asthma through sensitisation. The authors found a statistically significant annual excess of FEV_1 and FVC decline in workers exposed to a mean daily level of wood dust in the range of 0.2-0.4 mg/m^3/day (total dust), while exposure to >0.4 mg/m^3/day associated significantly only to FVC decline. Thus, a dose-response relationship between the estimated exposure and the annual decline was seen in FVC but not in FEV_1.[153] The authors did not report the gender of the participants, and its impact on the findings remains unknown. Second, the large 5-year longitudinal study of Glindmeyer et al. did not show an association between estimated average wood dust exposure and lung function changes in workers exposed to hardwood and softwood dusts in mean exposure levels in the range of 0.77-2.5 mg/m^3 (inhalable dust) and 0.10-0.23 mg/m^3 (respirable dust), excluding workers exposed to Western red cedar or other allergenic wood dusts.[67] Third, Bolund et al. 2018 in their 6-year follow-up found an

Table 13 Dose-response levels for nasal, respiratory and eye symptoms after exposure to inhalable wood dust in different studies (inhalable dust if not otherwise indicated).

Symptom	Exposure level (mg/m^3)[a]	OR (95% CI)	% with symptom		Reference
			Exposed	Controls	
Nasal symptoms					
Mucosal swelling or congestion	>0.74-1.42		NR	NR	185
	1.0-2.9[a] 3.0-4.9[a] 5.0-6.9[a] 7.0-9.9[a] ≥10[a]		11 25 31 46 63	NR	7
Blocked nose	2.04±1.53[a]		54	0	158
Runny nose	2.04±1.53[a]		24	0	158
	0.9-52.4, GM 3.9	2.3 (1.4-3.6)	11	5	178
General symptoms	0.1-4.6, median 0.6 0.2-9.8, median 1.0		43 49	NR	95
Respiratory symptoms					
Wheeze	>0.74-1.42	1.55 (1.08-2.22)	14	9	187
	0.9-52.4, GM 3.9	1.3 (0.8-2.0)	9	7	178
Night wheeze	>0.74-1.42	2.15 (1.15-4.02)	6	3	187
Cough	>0.74-1.42	1.40 (1.08-1.82)	26	15	187
	0.9-52.4, GM 3.9	1.6 (1.2-2.0)	51	40	178
	0.1-4.6, median 0.6 0.2-9.8, median 1.0		28 33	NR	95
Eye symptoms					
Irritation, itching, watering of eyes	0.9-52.4, GM 3.9	2.3 (1.4-4.6)	5	2	178
	≥2[a]		31	5-8	228
Itching	Mean 2.04±1.53[a]		41	0	158
Redness	Mean 2.04±1.53[a]		43	0	158
Conjunctivitis	0.1-4.6, median 0.6 0.2-9.8, median 1.0		7 9	NR	95

[a] concentration of total dust.

CI: confidence interval, OR: odds ratio, GM: geometric mean, NR: not reported.

association between cumulative wood dust exposure and decline in FEV_1 only among a relatively small subgroup of female wood workers but not among the larger group of male wood workers. The decline reached statistical significance in female workers exposed to >3.75 mg/m^3-years of inhalable wood dust during the follow-up,[18] corresponding to a mean exposure level of >0.63 mg/m^3 (inhalable dust).

There are also studies on cross-shift changes of lung function, but the evidence does not support the usefulness of cross-shift changes in predicting longitudinal lung function decline among woodworkers.[97] Holness et al. reported statistically significant cross-shift decline in FVC and FEV_1 among woodworkers exposed to mean dust levels of 1.83 mg/m^3 (total dust) and 0.29 mg/m^3 (respirable dust), when compared to controls.
No correlation between the level of wood dust exposure and the observed lung function decline over the work shift was detected.[88] Schlünssen et al. 2004 demonstrated a cross-shift change in FEV_1 among non-smoking woodworkers that was associated with estimated average exposure to wood dust.[189]

The usefulness of the several cross-sectional studies focusing on lung function among woodworkers is limited in assessing dose-response between wood dust exposure and lung function decline. A part of these studies indicates a negative association between estimated level of (total/inhalable) wood dust exposure and FEV_1, FVC and/or FEV_1/FVC.[48,100,128,129,216,228] In other studies, a negative association is reported between estimated cumulative exposure and FVC, FEV_1, and/or FEV_1/FVC.[9,234] There are also studies where such associations have not been found.[7,16,19,241,242] There were no systematic differences in the exposure levels in the cross-sectional studies indicating impaired lung function in comparison to those where these effects were not seen.

Overall, the evidence on wood dust exposure related lung function decline remains inconsistent, and further longitudinal studies would be needed to confirm the associations and clarify the dose-response relations. In the available studies, mean exposure levels ranging up to 2.5 mg/m^3 (inhalable dust) of other type of wood dust than Western red cedar was not found to cause lung function decline,[67] while in another study, exposure to >0.63 mg/m^3 (inhalable dust) was associated with lung function decline in a small subgroup of female wood workers but not in male.[18] Women may be more susceptible to wood dust related lung function decline than men, but further studies would be needed to confirm this. The potency of Western red cedar dust to cause lung function decline may differ from other types of wood dusts, as exposure in the range of 0.2-0.4 mg/m^3 of Western red cedar total dustwas associated with lung function decline (cohort likely to consist primarily of males).[153] This finding might be related to asthma caused by sensitisation to Western red cedar.

In conclusion, the evidence for an exposure-response relationship is inconsistent for lung function changes (Table 14).

11.3 Asthma

The meta-analyses of Pérez-Rios et al. and Zhang et al. indicate a 20-60% increase in asthma risk among workers occupationally exposed to wood dust, without providing further information on the dose-response.[166,243] Heikkilä et al. found increased asthma risk for low and medium exposure (total dust 0.02-<0.5 and 0.5-1.5 mg/m^3), but not for high exposure (≥1.5 mg/m^3) in their register-based study with 1,475 woodworkers. Healthy worker effect was suggested as an explanation for lacking dose-response ratio.[81] Schlünssen et al studied the risk of asthma verified with lung function tests. Asthma was related to dust level, most pronounced for symptomatic BHR among atopics at the highest inhalable dust level (>1.39 mg/m^3) compared with the lowest dust level (<0.80 mg/m^3).[186] However, there were only 54 participants with asthma symptoms and BHR.

Additionally, Vested et al. showed a more than twofold increase in the risk of hospital readmission in asthma patients occupationally exposed to wood dust during previous year, the risk being only slightly higher for persons with estimated mean inhalable dust exposure above 0.7 mg/m^3 than for those below 0.7 mg/m^3.[229]

To conclude, there is rather consistent evidence that wood dust exposure increases the risk of asthma development, but the knowledge on dose-response relations is minor. The risk seems to be most notable when wood dust level exceeds 1.39 mg/m^3 (inhalable dust),[186] but there is evidence on increased risk also below this level.[81] Atopy may increase the risk of asthma related to wood dust exposure.[186] Even low-level exposure to wood dust (below 0.7 mg/m^3 of inhalable dust) may exacerbate asthma and cause hospital readmission.[229]

In conclusion, the evidence for an exposure-response relationship is limited for asthma (Table 14).

11.4 Other pulmonary diseases

The evidence of causality between wood dust exposure and development of COPD is minor. In the 6-year follow-up study of Bolund et al. 2018, wood dust exposure at >0.63 mg/m^3 (inhalable dust) was associated with new-onset COPD in a small subgroup of smoking female wood workers but not in the larger cohort of male workers.[18]

Based on three meta-analysis of case-control studies an association between wood dust exposure and IPF is possible, but the significance of risks is probably modified by tobacco consumption. The risk of IPF may be higher in woodworkers exposed to hardwood. The knowledge on dose-

responses of wood dust related IPF is lacking because the data come from case-control studies without evaluation of exposure levels.[162,164,212]

In conclusion, the evidence for an exposure-response relationship is lacking for other pulmonary diseases than asthma (Table 14).

11.5 Carcinogenicity

Epidemiological studies provide consistent evidence on an association between cumulative wood dust exposure and nasal adenocarcinoma,[14,39,44,167,197,202] although studies addressing the exposure-response relations are scarce. A weaker association between non-adenocarcinoma sinonasal cancer and wood dust exposure is indicated in some studies.[14,202] There are also studies indicating an association between nasopharyngeal cancer and wood dust exposure in Asian study populations,[11,138] but these studies do not allow for further evaluation of exposure-response.

In the case-control study of Siew et al. 2017, including 393 cases of nasal adenocarcinoma, the HR for the lowest category of cumulative inhalable wood dust exposure (≤6.70 mg/m^3-years) was 3.16 (95% CI 2.08-4.81) and increased to 28.9 (95% CI 9.81-84.1) in the highest exposure category (≥28.82 mg/m^3-years). Adjustment for formaldehyde exposure decreased the HRs to 3.11 (95% CI 2.04-4.75) and 16.5 (95% CI 5.05-54.08), respectively. In both analyses, a dose-response relation was evident (p-trend <0.0001).[197] The subjects were exposed to both hardwood and softwood dust but since the study was carried out in the Nordic countries, softwood dust exposure is dominating.

The smaller case-control study of Pesch et al. 2008, including 86 cases of nasal adenocarcinoma, showed an OR 4.20 (95% CI 1.69-10.4) for their highest category of cumulative inhalable wood dust exposure (≥200 mg/m^3-years) as compared to the lowest exposure category (<140 mg/m^3-years).[167] One of the reasons for the lower risk estimate compared to the study of Siew et al. 2017[197] is that the reference category also had considerable exposure to wood dust. The increased risk was associated with hardwood dust exposure.

There are only few long-term inhalation studies in experimental animals (see Section 9.4). In these studies, beech dust exposure at 15-25 mg/m^3 did not induce nasal lesions in exposed rats.[87,210] Inflammation and lesions in the nasal cavity were reported in hamsters at 30 mg/m^3, but not at 15 mg/m^3.[49,236,237] In rats exposed at 18 mg/m^3, oak dust induced a potential increase in malignant lung tumours, and oak dust treated with sodium chromate in malignant nasal tumours.[108,109] These studies are too scarce to conclude dose-dependency.

Studies in wood dust exposed workers reported local genotoxicity in the buccal and nasal epithelium (see Section 10.3). Increased levels of biomarkers of oxidative stress and oxidative DNA damage were detected

at exposure levels of 1.48 mg/m^3 and 0.34 mg/m^3.[27,65] The lowest exposure level resulting in increased levels of micronuclei in buccal cells was 0.39 mg/m^3 [238] and in nasal cells 2.9±2.5 mg/m^3.[21] The studies also report other cellular changes in the nasal epithelium with the given exposure levels. Data do not allow distinction between softwood and hardwood exposures, and dose-response relationships were not investigated.

Regarding the exposure-response evidence for wood dust and carcinogenicity, two case-control studies[167,197] allowed an evaluation of the exposure-response (Table 14). However, the study by Pesch et al. (2008)[167] was small with only six cases in the reference category. In addition, the reference category in Pesch et al. (2008) had considerable wood dust exposure.

Among the earlier evaluations (Chapter 12), only the Dutch evaluation from year 2000 included a quantitative assessment of the cancer risk of occupational exposure to wood dust.[78] Based on the this evaluation, an excess risk of nasal cancer mortality of 4:100 000 would be reached at a cumulative exposure of 0.06 mg/m^3 (during 40 years) and concerns inhalable dust of a mix of hardwood and softwood typical in the Netherlands. The estimate was based on a linear risk model derived from the information of a very small number of nasal cancer deaths.[78]

Table 14 Conclusions on the exposure-response relationhip for each health effect.

Health effect	Evidence
Nasal, eye and respiratory symptoms	Limited
Lung function changes	Inconsistent
Asthma	Limited
Other pulmonary diseases	Not available
Carcinogenicity	Available

12 Previous evaluations by national and international bodies

International Agency for Research on Cancer (IARC) 1995 and 2012

In 1995, IARC classified wood dust as carcinogenic to humans (Group 1) based on strong evidence of an association between wood dust exposure and increased risk of sinonasal cancer.[92] In their evaluation in 2012, IARC concluded that there is consistent and strong evidence that wood dust causes sinonasal cancer. Among the studies that specified histology, very large excess risks were observed for sinonasal adenocarcinoma.[93]

According to IARC, there is also evidence, although weaker than for sinonasal cancer, that wood dust causes cancer of the nasopharynx. The majority of case-control studies observed an increased risk of cancer of the nasopharynx associated with wood dust exposure or with employment in wood-related occupations, although often based on small numbers. This is supported by the pooled re-analysis of cohort studies where a strong association was observed with probability of wood dust exposure. The primary confounder of concern was formaldehyde exposure, but in the pooled cohort study the probability of wood dust exposure, which would likely be inversely correlated with formaldehyde exposure, was associated with nasopharyngeal cancer risk, and an excess was observed among both the furniture workers and plywood workers subcohorts.

There was even weaker evidence for other sites such as the pharynx, larynx, and lung. Although positive associations were observed in some case-control studies, the patterns were not consistent and not supported by positive findings in cohort studies.

The great majority of studies did not report on the specific tree species to which workers were exposed or whether exposure was due primarily to hardwoods or softwoods. The few studies that did address tree species were relevant only for the evaluation of sinonasal cancer. According to IARC, there is strong evidence for an association between sinonasal cancer and exposure to hardwood dusts, based on the results of the few studies that specifically assessed exposure to hardwoods and on the results of case series that identified specific tree species. Among the few case-control studies that assessed the relationship with softwoods, there was a consistent excess risk, but the magnitude of the excess was smaller in comparison to hard-woods, and the association was primarily with squamous cell carcinoma.[92,93]

Scientific Committee for Occupational Exposure Limits (SCOEL) 2003

In their evaluation in 2003, SCOEL concluded that exposure to wood dust was shown to be associated with an increased risk of sinonasal cancer.[191] However, a quantitative risk assessment was not considered to be realistic because of the lack of good-quality quantitative data on exposure levels associated with increased risks. SCOEL indicated that very few studies have been conducted for workers exposed to average concentrations of wood dust lower than 0.5 mg/m^3 (total dust). Dust of Western red cedar was, however, considered to induce effects on the lower respiratory tract (asthma, bronchial hyperreactivity and lung function impairment) at these exposure levels. In the rare studies with exposure levels between 0.5 and 1 mg/m^3 of total dust, increase in the frequency of sinonasal symptoms and effects on the lower respiratory tracts (cough, chest tightness, lung function impairment and asthma) was indicated. At exposure levels higher than 1 mg/m^3 (total dust), clear health effects were indicated, including various symptoms of the upper respiratory tract, significant alteration of respiratory function parameters and asthma.

SCOEL concluded that that exposure above 0.5 mg/m^3 (total dust) induces pulmonary effects and should be avoided. Exposure levels lower than 0.5 mg/m^3 (total dust) were associated with the induction of bronchial asthma only when the exposure was to Western red cedar dust. The level of 0.5 mg/m^3 (total dust) and 1 mg/m^3 (inhalable dust) were considered to probably be below the levels to which the observed cases of sinonasal cancer had been exposed.[191]

Criteria Group for Occupational Standards, Sweden 2000

The Swedish Criteria Group concluded that the critical effect of occupational exposure to wood dust is irritation of eyes and upper respiratory passages with effects level from spruce and pine dust of 0.1-6.3 mg/m^3 wood dust. Additionally, wood dust can cause sinonasal adenocarcinoma (primarily based on studies of exposure to hardwood dust), while Western red cedar dust in the range 0.3-0.6 mg/m^3 has caused asthma, chronic decline in lung function and irritation of eyes and upper respiratory passages. Skin exposure to wood dust can cause both allergic and non-allergic contact eczema.[143]

Committee on the Evaluation of the carcinogenicity of chemical substances, Netherlands 2000

In their evaluation in 2000, the Committee on the Evaluation of the carcinogenicity of chemical substances under the Health Council of the Netherlands concluded that hardwood dust causes sinonasal adenocarcinoma in humans, and that there is also some epidemiological evidence on softwood dust causing sinonasal squamous-cell carcinoma.[78] The animal experimental data were evaluated not to provide any indication of carcinogenicity. According to the committee, hardwood and softwood dust extracts and condensates produce similar weak genotoxicity, which

relevance for the (possible) carcinogenicity of the dusts is questionable. Also, the inflammatory and cytotoxic potency of wood dusts was considered weak, and its relevance for the carcinogenicity unsettled. Since the carcinogenicity mechanisms of wood dusts are unresolved, the committee recommended using a linear model for calculating the excess lifetime cancer risks. Accordingly, the calculated excess risk for nasal cancer, based on a cohort mortality study among British furniture workers[3] and background nasal cancer risk in the Netherlands, was 1:25,000 for 40 years occupational wood dust exposure at 0.06 mg/m^3. The committee estimated a mean hardwood dust exposure level of 10 mg/m^3 for the cohort, based on the measured mean dust levels of 7.8 mg/m^3 in the 1970's and 4.2 mg/m^3 in the 1980's,[99] and considering the probably higher dust levels in the 1940's to 1960's. The cancer risk calculations were mentioned to address inhalable wood dust, although the dust fraction measured in the cited exposure assessment study[99] total dust, and no conversion from total to inhalable dust was presented.

German MAK Commission 1998

The evaluation of wood dust by the MAK Commission in 1998[45] was largely based on the IARC 1995 evaluation.[92] The committee concluded that exposure to beech and oak dust can induce nasal adenocarcinomas and probably also sinonasal squamous cell carcinomas. Dust of other hard-woods was considered potentially carcinogenic to humans, and softwood dust as well, although slightly less probably. Adequate information on the mechanisms of carcinogenicity or exposure-response was still missing. The committee noted that the existence of a threshold for tumour induction could not be excluded. Wood dust was considered to have sensitizing effects on the skin and respiratory tract.

The committee prepared separate evaluations of the allergenic effects of specific wood species.[46]

The following species were concluded to cause both skin and airway sensitisation:

- Western red cedar (*Thuja plicata*)
- Obeche (*Triplochiton scleroxylon*)

The following species were concluded to cause airway sensitisation:

- Afara (*Terminalia superba*)

The following species were concluded to cause skin sensitisation:

- Australian blackwood (*Acacia melanoxylon*)
- Cocus wood (*Brya ebenus*)
- Iroko (*Chlorophora excelsa*)
- East Indian rosewood (*Dalbergia latifolia*)
- African blackwood (*Dalbergia melanoxylon*)
- Brazilian rosewood (*Dalbergia nigra*)
- Cocobolo (*Dalbergia retusa*)
- Honduras rosewood (*Dalbergia stevensonii*)
- Ayan (*Distemonanthus benthamianus*)
- Australian silky oak (*Grevillea robusta*)
- African mahogany (*Khaya anthotheca*)

- Bolivian rosewood (*Machaerium scleroxylon*)
- African black walnut (*Mansonia altissima*)
- White peroba (*Paratecoma peroba*)
- Teak (*Tectona grandis*)

Dutch Expert Committee on Occupational Standards (DECOS) 1992

In 1992, the Dutch Expert Committee on Occupational Standards (a committee of the Ministry of Social Affairs; a predecessor of the current DECOS) recommended a health-based occupational exposure limit of 0.2 mg/m^3 (total dust, 8-hour TWA) for wood dust,[77] primarily based on preventing irritation of the eyes and respiratory tract. DECOS expected that prevention of eye and nose irritation also prevented the induction of nasal metaplasia. A clear distinction in health risks between different wood species could not be made. However, dust of Western red cedar was considered to cause occupational asthma at lower concentrations than dust of other wood species. In general, hardwood species were considered to constitute a greater health risk than softwood species.[77]

The American Conference of Governmental Industrial Hygienists (ACGIH) 2020

The ACGIH identified wood dust as a confirmed human carcinogen. Oak and Beech are confirmed human carcinogens; Birch, Mahogany, Teak and Walnut are suspected human carcinogens; and all other wood dusts are not classifiable as human carcinogens. The type of carcinogenicity is linked to sinonasal cancer and particularly adenocarcinoma. When determining a threshold limit value (TLV), a distinction was made between Western red cedar wood dust – which can trigger severe respiratory sensitization and asthma – and wood dust of all other wood species. A TLV of 0.5 mg/m^3 was deduced for the inhalable fraction of Western red cedar wood dust. A TLV of 1 mg/m^3 was deduced for the inhalable fraction of all other wood species in order to protect workers from the development of upper and lower respiratory tract irritation and respiratory function decreases.[1]

13 Evaluation of human health risks

13.1 Assessment of health risks

Occupational exposure to wood dust occurs in a wide variety of wood-related industries. It was estimated that the number of workers exposed to wood dust was around 3-4 million in the EU in 2000-2003, that represented approximately 2% of the workforce.[103] Epidemiological studies associate occupational exposure to wood dust with increased incidence of nasal adenocarcinoma and asthma, and with symptoms of the nose, eyes, skin and respiratory tract.

13.1.1 Genotoxicity and cancer

The available data provide strong evidence that wood dusts induce inflammatory reactions and production of ROS which contribute to the detected genotoxicity and cancer (see Appendix 2).

The available genotoxicity data indicate that both softwood and hardwood dusts are genotoxic, but do not allow conclusions on potential differences in potency. Reported human studies do not provide sufficient information to evaluate dose dependency of wood dust related genotoxicity. Increased levels of oxidative DNA damage and buccal micronuclei have been reported with inhalable wood dust exposure levels of 0.4 mg/m^3 and nasal micronuclei with exposure level of 3 mg/m^3.[21,65,238] It is inconclusive to which extent wood additives, endotoxins, co-exposure to other chemicals, and lifestyle factors such as smoking contribute to the observed genotoxicity in wood dust exposed workers.

Epidemiological studies show a strong dose-response association between wood dust exposure and nasal adenocarcinoma. The effect is especially evident for hardwood dust but also softwood dust appears to cause a clear excess risk. Although, based on the mechanistic data, inflammation related mechanisms are likely to contribute to the carcinogenicity of wood dust, a threshold or break-point in the exposure-response curve cannot be identified from the available data. The cancer risk seemingly starts to increase already from low levels of cumulative exposure. Calculation of exposure-response relations for nasal adenocarcinoma based on available epidemiolocal data is presented in Section 13.3.1.

Since nasal adenocarcinoma is an extremely rare disease, the number of cancer cases caused by wood dust remains small. The other cancer types, that have been studied as potentially associated with wood dust, are much more common but the role of wood dust in causation of these cancers seems to be non-existing or at least so small that it has not been possible to confirm it in the studies done so far.

13.1.2 Non-cancer health effects

Several different symptoms on nasal, eye and respiratory system have been reported in wood dust exposed workers. The data on irritative symptoms are mainly collected by questionnaires which decreases data precision since individuals may interpret the symptoms differently. Wood dust may also contain variable amounts of sensitising compounds, different additives, endotoxins, moulds and bacteria which may have an impact on the symptoms observed. The data do not allow for evaluating the impact of wood species, type of wood (dry/fresh) or woodworking methods on the observed symptoms. The potential dose-response relations for the symptoms are poorly addressed in most of the studies.

In the largest well-conducted study regarding irritation symptoms, including more than 2,000 Danish woodworkers, exposure to ≥1 mg/m^3 of inhalable wood dust was related to morning cough, daily coughing, and throat symptoms, when compared with the controls never exposed to wood dust.[185,187] In addition, inhalable wood dust exposure at >0.7-1.4 mg/m^3 was associated with wheeze, night wheeze, and daily coughing, in comparison to lower exposures at ≤0.7 mg/m^3, and with a significant increase in nasal congestion during the work shift, compared to before work. Workers exposed to inhalable wood dust levels below 1 mg/m^3 only had an increased risk of morning cough. The study has limitations by being cross-sectional, from one country only and largely based on self-reported symptoms. Still, data from this large woodworker study population is the best choice for assessing respiratory and irritative symptoms, as animal data (Chapter 9) does not allow for evaluation of these effects.

The evidence on lung function decline related to wood dust exposure remains inconsistent, and further longitudinal studies with adequate data on exposure levels are needed. In a study excluding wood types known to cause allergy, occupational exposure to inhalable wood dust levels up to 2.5 mg/m^3 did not result in lung function decline.[67] By contrast, exposure to relatively low levels of sensitising Western red cedar dust (0.2-0.4 mg/m^3 total dust) was associated with lung function decline.[153] This finding might be related to the asthma-causing potential of Western red cedar. Women may be more susceptible to wood dust-related lung function decline than men, as exposure to >0.6 mg/m^3 (inhalable dust) was shown to be associated with lung function decline in a small subgroup of female woodworkers but not in males.[18]

Occupational exposure to wood dust is likely to increase the risk of developing asthma (~1.5-fold increase reported in the studies).
The increased asthma risk is associated with high morbidity at the population level, as occupational exposure to wood dust is relatively common and up to about 9% of the working-aged population suffers from asthma.[83] However, the knowledge of the dose-response relationships is limited. The risk appears to be most evident when inhalable wood dust levels exceed 1.4 mg/m^3.[186] However, even lower level exposures (<0.5 mg/

m^3 total dust) have been shown to increase the risk of asthma in both genders.[81] Atopy may also increase the risk of wood dust exposure related asthma.[186] Furthermore, even low-level exposure to wood dust (below 0.7 mg/m^3 of inhalable dust) may exacerbate asthma and lead to hospital readmission.[229]

The evidence of causality between wood dust exposure and the development of COPD or IPF is limited. In one study, wood dust exposure at >0.6 mg/m^3 (inhalable dust) was associated with new-onset COPD in a small subgroup of smoking female woodworkers, but not in the larger cohort of male workers.[18] COPD is a common disorder, with a global prevalence around 10% among men aged 30-79 years, and <5% among women in the same age range.[4] By contrast, IPF is a rare disorder, usually observed in adults over the age of 50. It has a heterogeneous distribution and an incidence below 10 per 100,000 person-years. The impact of IPF may still be significant since it causes progressive lung fibrosis and early mortality.[164]

Wood dusts may cause irritative and allergic skin reactions although these are not frequently reported.[54]

13.2 Groups at extra risk

- **Smokers**: Some studies have reported higher risk of wood dust related adverse health effects such as COPD[18] and genotoxicity[26,175] among smokers than among non-smokers.
- **Atopics:** Atopy may increase the risk of asthma related to wood dust exposure.[186] This is an important finding because atopy, which is usually defined as having one or more IgE-mediated sensitisations to common aeroallergens like pollen and animal dander, is very common in industrial countries. In the study by Schlünssen et al.,[186] up to 45% of the workers had atopy, and generally, in population-based studies, one or even two-thirds of participants have been atopics.[139,160]
- **Asthmatics:** There is high prevalence of asthma among work-aged, even 10% or more of the workers may already have asthma. Wood dust exposure may exacerbate their disease. Notably, severe asthma exacerbations leading to hospital readmission have been reported to occur even with low-level exposure to wood dust.[229]
- **Women**: Women may be more susceptible to wood dust-related lung function decline and the development of COPD than men.[18] This is in line with the earlier suggestions that females tend to be more susceptible to the effects of cigarette smoke and other air impurities compared to males. Female smokers tend to present at a younger age and with a lower pack-year smoking history the same degree of lung function impairment compared to males. The possible mechanisms behind this are X-chromosomal genetic factors, hormonal factors, differences in airway growth, greater particle deposition in proximal airways among women, and inflammatory responses.[71,140]

13.3 Scientific basis for an occupational exposure limit

Epidemiological data provides sufficient evidence on nasal adeno-carcinoma and wood dust. In various cohort studies and case-control studies, excess risk of sinonasal cancer was observed after exposure to wood dust in general, and hardwood dust and softwood dust specifically.[92,93,177] The DECOS' subcommittee on Classification of carcinogenic substances was asked to recommend on the carcinogenic properties of wood dust, in particular on the distinction of hardwood and softwood dust. Its findings and considerations are summarised in Appendix 2. Taking into account the recommendation of the subcommittee, the committees are of the opinion that the available data do not allow conclusions on quantitative or relative differences in carcinogenicity between hardwood dust and softwood dust. Based on the available data on carcinogenic and genotoxic profile, the committees recommend to consider both hardwood dust and softwood dust as carcinogenic.
The committees note that in practice, exposure occurs to both hardwood dust and softwood dust, and the applied exposure measurement methods do not distinguish between hardwood and softwood dust. Therefore, the committees' health assessment applies to wood dust in general.

With regard to the mechanisms of action, there is evidence for genotoxicity mediated by ROS production. Indirect, inflammation-related mechanisms are likely to contribute to the carcinogenicity of wood dust. In addition, there are indications for genotoxicity caused by ROS generation at the surface of the wood particles, which is considered as a direct genotoxic mechanism of action (see Appendix 2). The relative contribution of indirect and direct genotoxic mechanisms of action cannot be determined. In such cases, a non-threshold approach is applied.

A further challenge that needs to be acknowledged is that wood dust is not a single agent but includes different types of wood species, differing in their physico-chemical properties, dust of both fresh and dry woods, and dust from untreated and chemically treated woods. This increases the uncertainty related to the representativeness of an OEL proposed based on specific data. Also, the particle size distribution of the dust may vary depending on the type of wood and woodworking methods applied. However, the committees are of the opinion that an overall uncertainty cannot be quantified and exhaustive evaluation of uncertainties is beyond the scope of the committees' task.

13.3.1 Calculation of excess cancer risk

Only two studies (Pesch et al. (2008) and Siew et al. (2017)) provide quantitative data on the relationship of cancer in humans and exposure to wood dust.[167,197] The study by Pesch et al. (2008) is a small study as only 6 cases were included in the reference category. A possible reason for the much lower risk estimate in Pesch et al. (2008) compared to Siew et al. (2017) is that in the former study, the reference category had considerable wood dust exposure. The case-control study of Siew et al. (2017) quantified the

cumulative wood dust exposure of a relatively high number of nasal adenocarcinoma cases and matched controls, who had an exposure profile relevant to Northern Europe. The committees note that this study also has limitations. The study population consists of males only, the work histories are derived from census data, and the exposure estimates are JEM-based, i.e. not addressing the exposure variability within occupations. Wood dust exposure in Nordic countries is softwood-dominant, but the exact fraction of hardwood dust exposure among the population remains unknown. Similarly, the exact fraction of exposure to impregnated wood dust is unknown, although expected to be low. There is, however, no specific evidence for increased nasal adenocarcinoma risk in relation to commonly used impregnants (e.g., copper, chromium, creosote). Overall, the study by Siew et al. (2017) is a well-designed study and was therefore selected for further excess risk calculations.

In line with the Guideline Calculation of cancer risk values[79] and previous advisory reports by the NEG and DECOS on diesel engine exhaust and respirable crystalline silica, exposure response modelling (using the best-fitting model) and life table analysis were applied for the calculation of cancer risk values.

An exposure-response function describing the relation between cumulative exposure to wood dust (in mg/m^3-years) and the hazard ratio (HR) for nasal adenocarcinoma was derived using the (individual-level) data from the case-control study performed by Siew et al. (2017). Exposure estimates were derived by linking occupational information obtained from census records to exposure estimates for wood dust from a job exposure matrix (the NOCCA JEM). Cumulative exposure was estimated from age 20 years until the index age of the case, for all subjects in a matched set, and conditional logistic regression was used to estimate exposure effects. The main analysis focuses on the effects of cumulative wood dust exposure with a lag of 10 years as was applied by Siew et al. (2017).

As there was substantial evidence for a non-linear exposure-response relation with a steeper slope at low cumulative exposures, a non-linear exposure-response model was fitted using a natural spline expansion with knots placed at the 25%, 50%, and 75% percentiles of the exposure distribution in exposed cases. Age-specific mortality rates were estimated using information on the average population size and number of deaths from all causes in 5-year age categories for the Dutch population during 2000-2014, as obtained from the Statistics Netherlands website (available online: www.cbs.nl).

Specific information on the age-specific incidence rates of nasal adenocarcinoma in the absence of wood dust exposure (the background incidence rate) were not available. Therefore, these rates were estimated based on available information on incidence rates of nasal cancer (ICD-10 code 30.0) in 5-year age categories during 2010-2020 as obtained from

the website of the National Cancer Registry in the Netherlands (NKR). A fraction of 12% of nasal cancers were assumed (for men and women combined) to be nasal adenocarcinomas, based on the proportion of nasal adenocarcinoma cases among all nasal cancer cases as reported by Kuijpens et al. (2018).[111]

A significant proportion of the recorded nasal adenocarcinomas may be related to occupational wood dust exposure. Considering the relatively high risk of wood dust exposure in the Nordic countries compared to the Netherlands, the attributable fraction of work-related nasal adenocarcinomas is expected to be higher in the Nordic countries. For the Nordic countries, an attributable fraction of 75% is assumed for nasal adenocarcinomas in men, and a smaller fraction in women. This corresponds to a probability of approximately 0.0025% in a not occupationally exposed population to develop nasal adenocarcinoma by the age of 75. No data were available on the contribution of occupational exposure to the incidence of adenocarcinomas in the Netherlands. The committees assume that the background rates in the Netherlands are comparable to the rates in the Nordic countries. With an expected cumulative incidence of nasal adenocarcinoma at age 75 in the absence of wood dust exposure that is equal to that estimated for the Nordic countries, the committees estimate that approximately 25% of the incidence of nasal adenocarcinoma in the Netherlands is work-related.

The committees estimate that the concentration of wood dust in air, which corresponds to an excess cancer risks of:

- 4 additional cases of nasal adenocarcinoma per 100,000 workers (4×10^{-5}), for 40 years of occupational exposure, equal to 0.1 mg/m^3 (target risk level or low risk level).
- 4 additional cases of nasal adenocarcinoma per 10,000 workers (4×10^{-4}), for 40 years of occupational exposure, equal to 0.8 mg/m^3.
- 4 additional cases of nasal adenocarcinoma per 1,000 workers (4×10^{-3}), for 40 years of occupational exposure, equal to 2.9 mg/m^3 (prohibition risk level or high risk level).

This is based on a life table calculation for the excess risk of nasal adenocarcinoma due to occupational exposure up to the age of 100 years. These risk-based HBC-OCRVs are expressed as 8-hour time-weighted average concentrations (8-hour TWA). The calculated concentrations apply to the inhalable fraction.

13.3.2 Considerations on non-cancer health effects

The committees note that the values in 13.3.1 relate to carcinogenic effects, for which no safe exposure threshold is assumed. In addition, exposure to wood dust is associated with the development of respiratory symptoms at comparable exposure ranges and for which a threshold is assumed. When setting an OEL for wood dust, it is important to consider also the associated non-cancer health effects. The committees note that the exposure-response data on non-cancer health effects are sparse and have inconsistencies

(summarised in Section 13.1.2). Of the available data, the most informative association with wood dust exposure was reported for upper and lower respiratory tract symptoms.[187] This study is a well conducted, reasonably large explorative cross-sectional study, but has various limitations inherent to the cross-sectional design and self-reporting of common and non-specific symptoms leading to a relatively high risk of bias.

Significantly increased symptoms among woodworkers compared to unexposed controls were morning cough, daily coughing, and throat symptoms. Waking up with chest tightness, waking up with wheeze and daily cough were reported more often by woodworkers with medium or high exposure compared to low exposed workers.

Notably, no association is found between exposure to wood dust and lung function, a more objective endpoint than the self-reported complaints. The committees further note that the exposure assessment approach has several limitations, including lack of precision and risk of systematic error due to particle size distribution captured by the passive samplers. Due to absence of a quantitative exposure-response relation, a no-observed adverse effect level (NOAEL) or a lowest-observed adverse effect level (LOAEL) cannot be determined based on the data reported.

Overall, the committees are of the opinion that the reported associations between respiratory symptoms and wood dust exposure do not allow the derivation of a reliable health-based OEL. However, although the available data on non-cancer respiratory effects of wood dust do not allow for a comprehensive evaluation of exposure-response relationships, there is limited evidence suggesting an increased risk of asthma development, asthma exacerbation, and respiratory symptoms at exposure levels around 1 mg/m^3 of inhalable wood dust.[185-187,229] This is in the range of the calculated concentrations for carcinogenic effects that correspond to risk levels of $4x10^{-4}$ and $4x10^{-3}$, the latter being the prohibitive risk level.

13.3.3 Measurement practises

It is recommended to measure the mass concentration of the inhalable dust fraction in the breathing zone of workers for the exposure assessment to wood dust. This fraction contains all inhaled particles, which is important since wood dust is known to cause health effects in the upper airways as well as in the lower parts of the respiratory tract. The dust samplers must comply with the inhalable dust conventions.[28,94]

13.3.4 Notations

Although there is evidence of respiratory sensitisation related to certain wood species, especially Western red cedar and certain tropical hard-woods, the mechanisms of the potential respiratory effects of other wood dusts are poorly understood. The rosin contained in coniferous wood dust, as well as the extractives of certain tropical hardwoods, may cause allergic contact dermatitis. Otherwise, wood dust does not typically cause allergic

dermatitis. Therefore, notation for skin or respiratory sensitisation is not recommended for wood dust in general. Skin notation is not recommended since wood dust is not expected to pass intact skin.

14 Research needs

Further in vivo and in vitro testing is required to establish clear understanding of the mechanisms of action leading to wood dust carcinogenicity. The reported genotoxicity studies in vitro have mainly been conducted in cell models representing lung epithelium, or in blood leukocytes. Further in vitro testing using sinonasal cell lines would be needed, as well as more studies analysing DNA and chromosomal damage in the nasal epithelium of wood dust exposed workers.

Better understanding of the molecular and cellular key events and adverse outcome pathways related to wood dust induced carcinogenicity could help to establish biomarkers for early health effects and provide means for identifying worker groups at risk.

Human studies mainly report mixed wood dust exposures. Better distinction of the wood species or identification of worker groups specialized to either hardwood or softwood processing would help to conclude if hardwood species constitute different health risks compared to softwood species. Alternatively, well-executed (and reported) in vivo studies following the recommended standardized test methods for the detection of genotoxicity could help to understand if softwood and hardwood dusts possess similar genotoxic potential. Also, the impact of different types of impregnating agents on the toxicological properties of wood dust remains unresolved.

Despite the large number of human studies available, information on exposure-response relations of wood dust is still scarce. Further high-quality epidemiological studies would be needed to address the exposure-response relations of wood dust related carcinogenicity, as well as of non-malignant pulmonary effects related to wood dust exposure.

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Appendix 1

Occupational exposure limits

Table A1.1 Occupational exposure limits for wood dust in various countries.

Country	Substance	8-h OEL (TWA) mg/m³	Fraction	Notation/Comment	Ref.
Australia	Wood dust (certain hardwoods such as beech & oak) Wood dust (soft wood)	1 5	Inh.	Sen Sen, STEL 10 mg/m³	208
Denmark	Wood dust	1	Inh.	C, STEL 2 mg/m³	50
EU	Hard wood dust [a]	2	Inh.	-	55
Finland	Wood dust [b]	2	Inh.	-	195
Germany (AGS)	Hardwood dust [a]	2	Inh.	-	5
Germany (DFG)	Beech wood dust Oak wood dust Wood dust (except beech and oak wood dust)	- - -	- - -	Carc cat 1 Carc cat 1 Carc cat 3	46
The Netherlands	Hard wood dust	2	Inh.	C	192
Norway	Wood dust from hard exotic woods, oak and beech [a] Wood dust from Nordic wood species except oak and beech	1 2	Inh. Total	C C	152
Sweden	Hard wood dust Soft wood dust	2 2	Inh. Inh.	C -	209
UK	Hard wood dust [a] Soft wood dust [c]	3 5	Inh. Inh.	C, Sen Sen	89
US (ACGIH)	Western red cedar All other species	0.5 1	Inh. Inh.	DSEN, RSEN; A4 -¤	2
US (NIOSH)	Hard wood dust, soft wood dust, Western red cedar dust	1	-	10-h TWA	151
US (OSHA)	Wood dust	15 5	Total Resp.	- -	157

[a] If hardwood dusts are mixed with other wood dusts, the limit value shall apply to all wood dusts present in that mixture.

[b] For new and renovated facilities the value 1 mg/m3 is applied.

[C] If softwood dusts are mixed with hardwood dusts, the WEL for hardwood dusts shall apply to all the wood dusts present in that mixture.

A4: not classifiable as a human carcinogen, ACGIH: American Conference of Governmental Industrial Hygienists, AGS: Ausschuss für Gefahrstoffe (Committee on Hazardous Substances), C: carcinogen, Carc cat 1: substances that cause cancer in man and can be assumed to contribute to cancer risk, Carc cat 3: substances that cause concern that they could be carcinogenic for man but cannot be assessed conclusively because of lack of data, DFG: Deutsche Forschungsgemeinschaft (German Research Foundation), DSEN: dermal sensitiser, EU: European Union, Inh.: inhalable, NIOSH: National Institute for Occupational Safety and Health, OEL: occupational exposure limit, OSHA: Occupational Safety and Health Administration, Resp: respirable, RSEN: respiratory sensitiser, Sen: sensitiser, STEL: short-term exposure limit, TWA: time-weighted average.

Appendix 2

Advice of the Subcommittee on Classification of Carcinogenic Substances

Background

The Dutch Expert Committee on Occupational Safety (DECOS) has requested the Subcommittee on Classification of carcinogenic substances (hereafter referred to as 'committee') to comment on the carcinogenic classification of wood dust (in particular the distinction of hardwood and softwood) and the mode of carcinogenic action. The subcommittee's findings and considerations are summarised below.

Carcinogenicity of hardwood and softwood

In 1998, the Health Council has recommended to classify hardwood in category 1. For softwood, insufficient data were available. Therefore, only hardwood has been included in the CMR-list of the Dutch Ministry of Social Affairs and Employment. The Health Council decided not to discriminate between hardwood and softwood in its advisory report of 2000, in which it derived a recommended exposure limit. The main reason for this decision was the similarity of the genotoxic response observed for hardwood and softwood dust. More recently, the IARC, and also the NEG and DECOS in the present report, evaluate wood dust without further discrimination of wood type.

For the current evaluation, it is relevant to determine whether hardwood and softwood can be distinguished with respect to its carcinogenic properties. Although fibre length differs between hardwood and softwood, especially the type of processing (polishing, sanding, sawing, heating) influences the particle size of wood dust. Particle size seems to be of importance as differences in particle size can lead to differences in effect in the airways. From the evidence summarised in the NEG-DECOS report, it appears that the inhalable fraction is most relevant due to the effects observed in the upper airways. The subcommittee notes that in general, in epidemiological literature the type of wood is not specified and no distinction is made between exposures to hardwood and softwood. Additionally, in occupational practise exposure occurs often to both hardwood and to softwood dust. For these reasons it is generally not possible to assign the observed health effects to a specific type of wood.

Conclusion

The committee concludes that insufficient data are available to discern hardwood from softwood dust, with respect to the carcinogenic properties.

Mechanism of action

Genotoxicity and generation of reactive oxygen species (ROS) after exposure to (mainly wood extracts of) hardwoods and softwoods have been tested in in vitro and in vivo studies. In most studies positive responses were noted, however no clear differences between hardwoods and softwoods were observed (Table 11 from the NEG-DECOS report).

The subcommittee has evaluated the data from Chapter 8 Mechanism of toxicity of the NEG-DECOS report to determine the mode(s) of action of wood dust (see Table 2 for more details on the references used in this chapter). The available data clearly indicate that inflammation, and subsequent generation of ROS, play a role in the genotoxic and carcinogenic effects of wood dust. The subcommittee considers ROS-generation via inflammation as an indirect mechanism of action. Involvement of direct mechanisms of action have also been suggested, including ROS-generation at the particle surface, DNA-damage by physical interaction and mutagenicity by chemicals isolated from wood extracts. When no experimental data are available on a threshold, the subcommittee assesses genotoxic carcinogens that generate ROS as direct genotoxic carcinogens (80). The subcommittee notes that based on the available data, it is not clear which direct mechanism is involved, and to what extent it contributes to the observed genotoxic response. As a consequence of the uncertainty related to the involvement of direct modes of action and the presence of a genotoxic threshold, the Health Council applies a non-threshold (risk-based) approach.

Conclusions

The subcommittee concludes that the genotoxicity data do not indicate a clear difference between hardwood and softwood in either potency or mechanism of action. The genotoxicity data indicate that in addition to indirect genotoxicity caused by inflammation, direct mechanisms of action could be involved. The possibility of a direct genotoxic mechanism contributing to the carcinogenic effects of wood dust should therefore be taken into account.

Table A2.1 Committee's interpretation of studies referenced in the NEG-DECOS report with respect to the genotoxic mode of action.

Reference	Description from NEG report	Mechanism (direct, indirect, non-genotoxic)
Bornholdt et al. 2007[20]	"In vitro experiments have shown that the potency of different wood dusts in inducing DNA damage and inflammatory interleukins do not correlate, which suggests that the observed genotoxicity of the studied wood dusts is independent of the cytokine-induced inflammation."	Appears to support a direct mechanism of action, since there is no correlation between DNA damage and inflammation.
IARC 1995[92]	"Also, direct genotoxic effects of wood dust extracts have been reported in older studies summarised by IARC (1995)."	Extracts shown positive results in an Ames test support a direct mode of action.
Staffolani et al. 2015[204]	"Hardwood and pine dusts were cyto-genotoxic and able to induce oxidative DNA damage in vitro in human bronchial epithelial BEAS-2B cells and there was an association with a delay of DNA repair resulting in accumulation of DNA lesions."	Direct/indirect
Pylkkänen et al. 2009[171]	"Exposure to pine, birch and oak dusts induces cytotoxicity and ROS production in BEAS-2B cells indicating that ROS-related mechanisms are involved in wood dust toxicity in human airway epithelial cells."	Not clear whether ROS production is caused by a direct or indirect mechanism.
Rekhadevi et al. 2009[175]	"Decreased levels of superoxidase dismutase were measured in wood dust exposed workers indicating antioxidant stress due to increase in ROS. The exposed workers also had increased levels of DNA and chromosomal damage in peripheral blood leukocytes as well as increased level of micronuclei din buccal cells."	Not clear whether ROS production is caused by a direct or indirect mechanism.
Cellai et al. 2019[27]	"An association was shown between wood dust and oxidative DNA damage (M1dG adducts in nasal epithelium and urinary 15-F2t-isoprostane)"	M1Dg adducts are only formed after lipid peroxidation, which suggests an indirect mechanism of action.
Ghelli et al. 2021[65]	"and biomarkers of oxidative stress (15-F2t-isoprostane and 8-oxo-dGuo) were significantly correlated with exposure to wood dust."	Not clear whether ROS production is caused by a direct or indirect mechanism.
Naarala et al. 2003, Long et al. 2004[126,148]	"It has been demonstrated that in alveolar macrophages pine dust stimulates the generation of ROS."	Inflammation; an indirect mechanism of action
Tao et al. 2003[211]	"ROS have been shown not only to damage cells by peroxidising lipids and disrupting DNA and proteins, but also to exert signalling functions and modulate gene transcription."	Not clear whether ROS production is caused by a direct or indirect mechanism.
Llorente et al. 2009[125]	"One proposed mechanism for the carcinogenicity of wood dust is reduced clearance of particles from the sinonasal cavity, leading to mechanical irritation, inflammation, and increased cell proliferation. To support this, increased nasal mucociliary clearance time has been reported in wood industry workers (Chapter 6)."	Inflammation; an indirect mechanism of action
Tátrai et al. 1995[213]	"The idea of several contributing factors, such as local irritation, free-radical generation, and consequences of microbial contamination, was also suggested by Tátrai et al. (1995). Secondary genotoxicity, mediated by inflammatory reaction, is likely to contribute to the carcinogenicity of wood dust. Chronic inflammation is suspected to contribute to the initiation and progression in various cancers, and studies presented in Section 9.2 confirm that wood dust induces inflammatory response in lungs in vivo."	Inflammation; an indirect mechanism of action [The committee recommends to exclude this study due to the involvement of microbial contamination]
Cellai et al. 2019[27]	"Cellai et al. (2019) proposed that free radicals produced by inflammatory reaction as a consequence of wood dust could play a major role in the development of sinonasal cancer.	Inflammation; an indirect mechanism of action

Appendix 3

Life table analysis

Lifetable analyses for occupational wood dust exposure and excess risk of nasal adenocarcinoma

Report for the Dutch Health Council, August 2025

Prepared by Dr. Lützen Portengen

Institute for Risk Assessment Sciences (IRAS), Utrecht University

Data sources

The main data sources used to perform this lifetable analysis were:

1. An exposure-response function describing the relation between cumulative exposure to wood dust (in mg/m^3-years) and the hazard ratio (HR) for nasal adenocarcinoma was derived using the (individual-level) data from the case-control study performed by Siew et al. 2017.[197] Exposure estimates were derived by linking occupational information obtained from census records to exposure estimates for wood dust from a job exposure matrix (the NOCCA JEM). Cumulative exposure was estimated from age 20 years until the index age of the case, for all subjects in a matched set, and conditional logistic regression was used to estimate exposure effects. The main analyses focused on the effects of cumulative wood dust exposure with a lag of 10 years, but results from an exposure-response model fitted to exposures with a lag of 20 years are provided as a sensitivity analysis (S1). An analysis based on categories of exposure provided clear evidence of a non-linear exposure-response relation with relatively higher (log-)Hazard Ratios at low cumulative exposures (Figure A3.2). The main analysis was therefore based on a non-linear exposure-response model, which was fitted using a natural spline expansion with knots placed at the 25%, 50%, and 75% percentiles of the exposure distribution in exposed cases. An exposure-response model fitted under the assumption of a linear relation between exposure and the log-hazard resulted in an estimated Hazard Ratio (HR) [95% CI] of 1.09 [1.07, 1.10] per mg/m^3-years of wood dust. Results from a life table analysis based on this linear exposure-response relation are presented as a sensitivity analysis (S2).
2. Age-specific mortality rates were estimated using information on the average population size and number of deaths from all causes in 5-year age categories for the Dutch population during 2000-2014. as obtained from the Statistics Netherlands website (available online: www.cbs.nl).
3. Specific information on the age-specific incidence rates of nasal adenocarcinoma in the absence of wood dust exposure (the background incidence rate) was missing and were therefore estimated from available information on incidence rates of nasal cancer (ICD10 code 30.0) in 5-year age categories during 2010-2020 as obtained from the website of the National Cancer Registry in the Netherlands (NKR). We assumed that 12% of nasal cancers were nasal adenocarcinomas, based on the proportion of nasal adenocarcinoma cases among all nasal cancer cases

as reported in Kuijpens et al. 2018.[111] Because a significant proportion of the recorded nasal adenocarcinomas may be related to occupational wood dust exposure, the background incidence rate of nasal adenocarcinoma was estimated under the assumption that approximately 25% of the incidence of nasal adenocarcinoma was work-related. This proportion was derived under the assumption that background rates in the Netherlands should be comparable to that in the Nordic countries, and more specifically that the expected cumulative incidence of nasal adenocarcinoma at age 75 in the absence of wood dust exposure should be equal to that used by the NEG.

Based on a lifetable analysis, the wood dust exposure levels were estimated that are expected to result in 4 additional cases of nasal adenocarcinoma after 40 years of occupational exposure, from age 20-60 years, at age 100 years, either per 1,000 workers ($4x10^{-3}$; prohibitive risk level) or per 100,000 workers ($4x10^{-5}$; target risk level).

All analyses were conducted using R version 4.5.1.

Results

Figure A3.1 visualizes the estimated exposure-response relation (A), the age-specific mortality rate (B), and the estimated incidence rate of nasal adenocarcinoma in the absence of wood dust exposure (C) for the main analysis.

Table A3.1 shows the estimated wood dust exposure levels corresponding to the two different excess risk levels for the main analysis.

Table A3.2 shows the estimated wood dust exposure levels corresponding to the two different excess risk levels for the sensitivity analyses S1 and S2.

Table A3.1

Risk level	Wood dust exposure (mg/m3)
4/100,000	0.10
4/10,000	0.79
4/1,000	2.91

Table A3.2

Sensitivity analysis	Risk level	Wood dust exposure (mg/m3)
S1: Lag 20 years (non-linear exposure-response relation)	4/100,000	0.11
	4/1,000	3.30
S2: HR=1.09 per mg/m3-yrs	4/100,000	0.25
	4/1,000	1.51

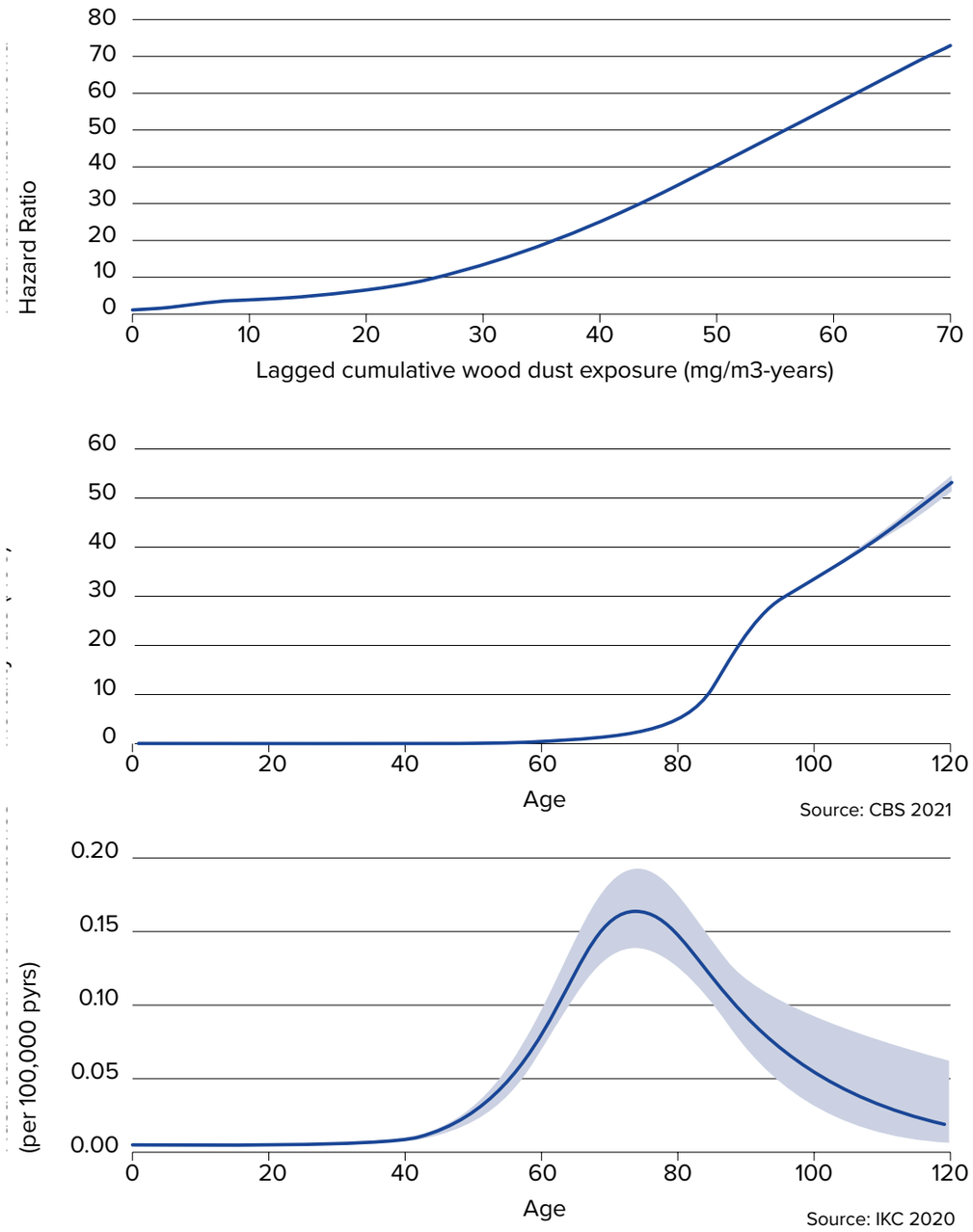

Figure A3.1 Estimated exposure-response relation between cumulative wood dust exposure and the Hazard Ratio for adenocarcinoma based on a lag of 10 years (A), the age-specific all-cause mortality rate (B), and age-specific incidence rate of adenocarcinoma in unexposed (C).

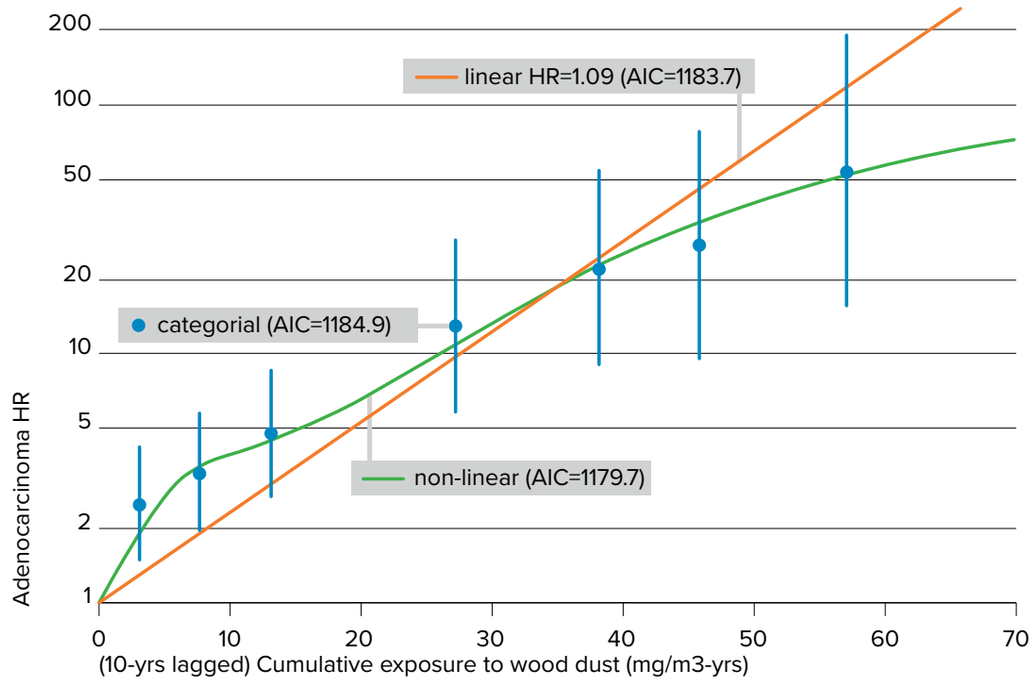

Figure A3.2 Fitted exposure-response relations using categories of exposure, a linear model, and a non-linear model using a regression spline. Akaike's Information Criterion (AIC) was included as a measure of model fit (lower is better). The vertical axis is plotted on the log-scale to conform to the log-linear relation assumed by the statistical model.

Committees and consulted experts

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The Nordic Expert Group – appointment and interests procedures

Members of the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG) are appointed by the Director General of the Swedish Work Environment Authority (SWEA) following nominations from the Danish, Finnish, Norwegian and Swedish occupational health institutes. They are appointed in a personal capacity because of their special expertise in relevant areas. NEG does not follow a formal procedure regarding conflict of interest, however, being employed by state institutes, the members are obliged to report any potential conflict of interest. See also nordicexpertgroup.com for more information about the procedures of NEG.

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[a] Observers and consulted experts are entitled to speak during the meeting. They do not have any voting rights and do not bear any responsibility for the content of the Committee's advisory report.

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The Health Council receives most requests for advice from the Ministers of Health, Welfare and Sport, Infrastructure and Water Management, Social Affairs and Employment, and Agriculture, Fisheries, Food Security and Nature. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.
Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity.
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This advisory report has been offered to the Minister of Work and Participation by Prof. R. Lindauer, vice chair of the Health Council.

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