FINAL

Report on Carcinogens Background Document for

Wood Dust

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Report on Carcinogens Subcommittee

Prepared for the:
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Criteria for Listing Agents, Substances or Mixtures in the Report on Carcinogens

U.S. Department of Health and Human Services
National Toxicology Program

Known to be Human Carcinogens:

There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance or mixture and human cancer.

Reasonably Anticipated to be Human Carcinogens:

There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible but that alternative explanations such as chance, bias or confounding factors could not adequately be excluded; or

There is sufficient evidence of carcinogenicity from studies in experimental animals which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors: (1) in multiple species, or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site or type of tumor or age at onset; or

There is less than sufficient evidence of carcinogenicity in humans or laboratory animals, however; the agent, substance or mixture belongs to a well defined, structurally-related class of substances whose members are listed in a previous Report on Carcinogens as either a *known to be human carcinogen, or reasonably anticipated to be human carcinogen* or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub populations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.

Summary Statement

Wood Dust

Carcinogenicity

Wood dust is *known to be a human carcinogen*, based on sufficient evidence of carcinogenicity from studies in humans. It has been demonstrated through human epidemiologic studies that exposure to wood dust increases the occurrence of cancer of the nose (nasal cavities and paranasal sinuses). An association of wood dust exposure and cancers of the nose has been observed in numerous case reports, cohort studies, and case-control studies specifically addressing nasal cancer. Strong and consistent associations with cancer of the nasal cavities and paranasal sinuses were observed both for occupations associated with wood dust exposure and for directly estimated wood dust exposure. Risks were highest for adenocarcinoma, particularly among European populations. Studies of U.S. populations also showed similar significant positive associations. A pooled analysis of 12 case-control studies showed a dose-response pattern, with estimated relative risk for adenocarcinoma reaching 45.5 (95% CI = 28.3-72.9) in highly exposed males (Demers *et al*. 1995). The association of wood dust exposure with elevated nasal cancer risk in a large number of independent studies and with many different occupations in many countries argues strongly that the elevation was due to wood dust rather than other concurrent exposure(s) such as formaldehyde or wood preservatives.

Other types of nasal cancers (squamous cell carcinoma of the nasal cavity) and cancers at other sites, including the nasopharynx, the larynx, and Hodgkin's disease have been associated with wood dust exposure in several epidemiologic studies. However, these findings were positive in some but not in all studies and the overall epidemiologic evidence lacks the strength and consistency to draw firm conclusions about the role of wood dust exposure and cancer at these other sites.

There is inadequate evidence for the carcinogenicity of wood dust from studies in experimental animals. No tumors attributable to beech wood dust exposure were found in inhalation studies in female Sprague-Dawley rats, female Wistar rats, or male Syrian golden hamsters, or in intraperitoneal injection studies in female Wistar rats. Similarly, inhalation exposure of wood dust did not significantly affect the incidence of tumors induced by formaldehyde in female Sprague-Dawley rats, sidestream cigarette smoke in female Wistar rats, or N-nitrosodiethylamine in male Syrian golden hamsters. Each of these studies suffers from various limitations such as small numbers of animals and dose groups, short study duration, and inadequate data reporting.

Other Information Relating to Carcinogenesis or Possible Mechanisms of Carcinogenesis

An increased frequency of DNA damage and micronuclei has been observed in peripheral blood lymphocytes from humans exposed occupationally to wood dust.

Dermal exposure to a methanol extract of beech wood dust resulted in a significant increase in skin tumors (squamous cell carcinoma, papilloma) and mammary tumors (adenocarcinoma, adenoacanthoma, mixed tumors) in female NMRI mice. Weak positive results for reverse mutations in *Salmonella typhimurium* have been reported for polar organic solvent extracts of some hardwood dusts, particularly beech. In addition, two chemicals found in wood, Δ^3 carene and quercetin, were found to be mutagenic in *Salmonella*. *In vitro* and *in vivo* tests with polar organic solvent extracts of some wood dusts (beech and oak) in mammalian systems have shown positive results for DNA damage (primarily single-strand breaks and repair), micronucleus induction, and chromosomal aberrations (primarily chromatid breaks).

The role of specific chemical components of the wood (naturally occurring or exogenously added compounds) in wood dust-induced carcinogenesis is unclear. The particulate nature of wood dust may also contribute to wood dust-associated carcinogenesis since dust generated by wood working typically consists of a high proportion of particles that are deposited in the nasal cavity. Chronic exposure to wood dust particulates is associated with decreased mucociliary clearance and enhanced inflammatory reactions in the nasal cavity in some studies in humans. Additionally, cellular changes (metaplasia and dysplasia) observed in the nasal mucosa of wood workers and laboratory animals may represent preneoplastic states.

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1 Introduction

Wood dust was nominated for listing in the Report on Carcinogens by the Occupational Safety and Health Administration (OSHA), based on the 1995 International Agency for Research on Cancer (IARC) monograph, which concluded that there was sufficient evidence of carcinogenicity in humans for wood dust and classified it as *carcinogenic to humans* (Group 1) (IARC 1995). The IARC listing was based on evidence from human studies that reported increased risk of cancer of the nasal cavities and paranasal sinuses associated with exposure to wood dust.

Wood is an important worldwide renewable natural resource. Forests comprise approximately one-third of the earth's total land mass (~3.4 million km^2). There are an estimated 12,000 species of trees, each producing a characteristic type of wood. Consequently, there is considerable variation in the species of trees harvested in different countries and, in some cases, in different parts of a single country. However, even in countries that have high domestic production of wood, some wood may be imported for specific uses such as furniture production (IARC 1995).

Based on seed type, spermatophytes are subdivided into two classes: gymnosperms (which have exposed seeds), and angiosperms (which have encapsulated seeds). Most tree species are deciduous trees, or hardwoods, principally angiosperms. Only about 800 species are coniferous trees, or softwoods, principally gymnosperms (Bauch 1975). However, softwood species account for about two-thirds of all industrial uses of wood (IARC 1995).

The terms "hardwood" and "softwood" refer to the species, and not necessarily the hardness of the wood. Although hardwoods generally are more dense than softwoods, the density varies considerably within each group, and the hardness of the two groups overlaps somewhat (Fengel and Wegener 1989, cited in IARC 1995). The scientific and common names of some softwood and hardwood trees are compiled in Table 1-1 (Vaucher 1986, cited in IARC 1995).

Table 1-1. Scientific and common names for softwood and hardwood trees

Common names	Genus and species
Softwood	
Spruce	*Picea*
Pine	*Pinus*
Fir	*Abies*
Larch	*Larix*
Cedar	*Chamaecyparis*
Douglas fir	*Pseudotsuga menziesii*
Redwood	*Sequoia sempervirens*
Hemlock	*Tsuga*

Common names	Genus and species
Hardwood	
Chestnut	*Castanea*
Walnut	*Juglans*
Hickory	*Carya*
Beech	*Fagus*
Oak	*Quercus*
Aspen, poplar	*Populus*
Ash	*Fraxinus*
Birch	*Betula*
Maple	*Acer*
Sycamore	*Platanus*
Cherry	*Prunus*
Willow	*Salix*
Elm	*Ulmus*

Source: Vaucher 1986, cited in IARC 1995

Wood dust is generated when timber is processed, such as when it is chipped, sawed, turned, drilled, or sanded.

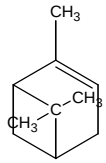
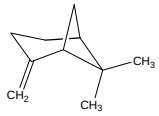
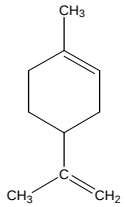
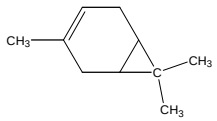
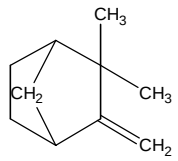
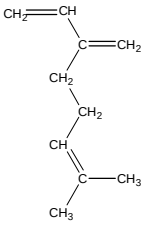
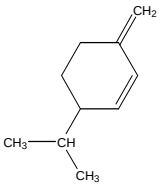
1.1 Chemical identification

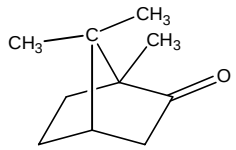
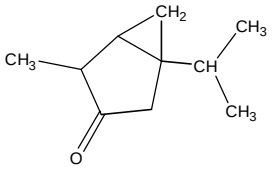
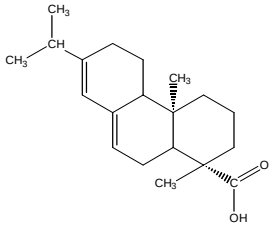
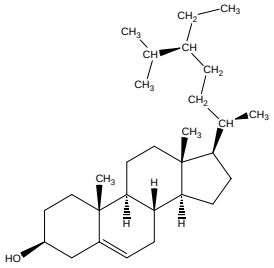
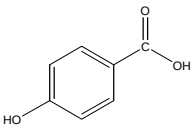
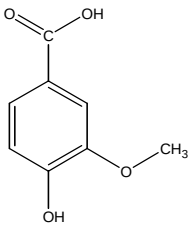
Wood dust is a complex mixture. Its chemical composition depends on the species of tree and consists mainly of cellulose, polyoses, and lignin, with a large and variable number of substances with lower relative molecular mass. Cellulose is the major component of both softwood and hardwood. Polyoses (hemicelluloses) are present in larger amounts in hardwood than in softwood. They contain five neutral sugar units: hexoses, glucose, mannose, galactose, and the pentoses (xylose and arabinose). The lignin content of softwood is higher than that of hardwood. The monomers of lignin are phenylpropane units joined by various linkages.

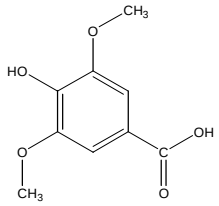
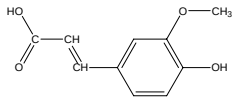
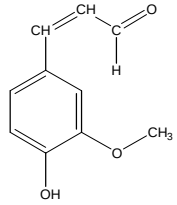
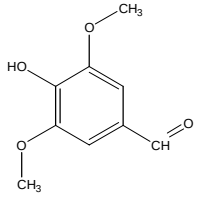
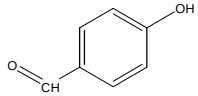
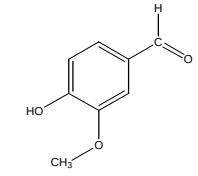
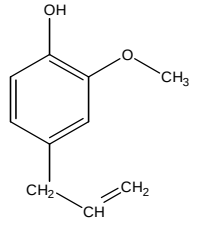
The lower-molecular-mass substances significantly affect the properties of wood; these include substances extracted with nonpolar organic solvents (fatty acids, resin acids, waxes, alcohols, terpenes, sterols, steryl esters, and glycerols), substances extracted with polar organic solvents (tannins, flavonoids, quinones, and lignans), and water-soluble substances (carbohydrates, alkaloids, proteins, and inorganic material). Hardwood tends to have a higher percentage of polar-soluble substances than softwood.

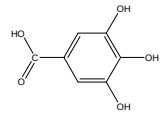
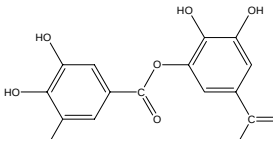
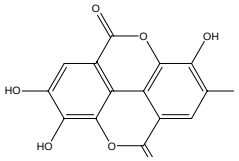
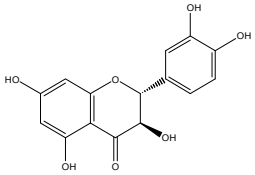
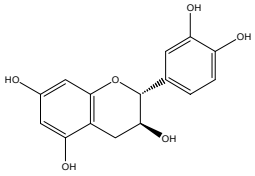
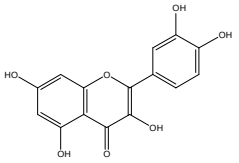
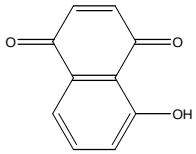
The main constituents of woods are summarized in Table 1-2 (IARC 1995). The IARC monograph cited extensive reviews, with detailed accounts of numerous extractives (Beecher *et al.* 1989, Fengel and Wegener 1989, Swan 1989).

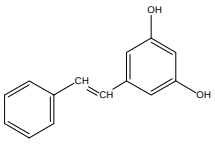
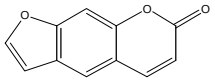
Table 1-2. Certain natural chemical components of softwood and hardwood

Chemical Name	CASRN	Molecular Weight	Structure
α-Pinene $C_{10}H_{16}$	80-56-8	136.24	
β-Pinene $C_{10}H_{16}$	127-91-3	136.24	
Limonene $C_{10}H_{16}$	138-86-3	136.24	
delta-3-Carene $C_{10}H_{16}$	13466-78-9	136.24	
Camphene $C_{10}H_{16}$	79-92-5	136.24	
Myrcene $C_{10}H_{16}$	123-35-3	136.24	
β-Phellandrene $C_{10}H_{16}$	555-10-2	136.24	

Chemical Name	CASRN	Molecular Weight	Structure
Camphor $C_{10}H_{16}O$	76-22-2	152.24	
Thujone $C_{10}H_{16}O$	546-80-5 471-15-8	152.24	
Abietic acid $C_{20}H_{30}O_2$	514-10-3	302.46	
β-Sitosterol $C_{29}H_{50}O$	83-46-5	414.71	
p-Hydroxybenzoic acid $C_7H_6O_3$	99-96-7	138.12	
Vanillic acid $C_8H_8O_4$	121-34-6	168.15	

Chemical Name	CASRN	Molecular Weight	Structure
Syringic acid $C_9H_{10}O_5$	530-57-4	198.18	
Ferulic acid $C_{10}H_{10}O_4$	1135-24-6	194.19	
Coniferyl aldehyde $C_{10}H_{10}O_3$	458-36-6	178.19	
Syringaldehyde $C_9H_{10}O_4$	134-96-3	182.18	
p-Hydroxy-benzaldehyde $C_7H_6O_2$	123-08-0	122.12	
Vanillin $C_8H_8O_3$	121-33-5	152.15	
Eugenol $C_{10}H_{12}O_2$	97-53-0	164.20	

Chemical Name	CASRN	Molecular Weight	Structure
Gallic acid $C_7H_6O_5$	149-91-7	170.12	
Digallic acid $C_{14}H_{10}O_9$	536-08-3	322.23	
Ellagic acid $C_{14}H_6O_8$	476-66-4	302.20	
Taxifolin $C_{15}H_{12}O_7$	480-18-2	304.26	
Catechin $C_{15}H_{14}O_7$	154-23-4	290.27	
Quercetin $C_{15}H_{10}O_7$	117-39-5	302.24	
Lapachol $C_{15}H_{14}O_3$	NA	242.27	NA
Juglone $C_{10}H_6O_3$	481-39-0	174.16	

Chemical Name	CASRN	Molecular Weight	Structure
Pinosylvin $C_{14}H_{12}O_2$	102-61-4	212.25	
Psoralen $C_{11}H_6O_3$	66-97-7	186.17	

Source: IARC 1995

NA: not available.

1.2 Physical-chemical properties

Wood dust is a light brown or tan fibrous powder. Its specific gravity is 0.56 (Radian 1991). The morphology of softwood tissue is simpler than that of hardwood. The bulk of softwood consists of just one type of cell, tracheids. Tracheids are elongated fiber-like cells with a square or polygonal cross-section. Less than 10% of the wood consists of short, brick-like parenchymal cells arranged radially. Softwoods contain epithelial cells that secrete resin into canals, which run horizontally and radially through the wood.

In hardwoods, there is more detailed differentiation between stabilizing, conducting, and storage tissue. Stabilizing tissues contain libriform fibers and fiber tracheids, which are elongated cells with thick polygonal walls and small lumina. The conducting system is composed of vessel elements fitted together to form long tubes of up to several meters. The vessels have thin walls and large diameters. Hardwoods that contain resin canals also have a secretory system of epithelial cells (IARC 1995). Certain characteristics of softwood and hardwood are compared in Table 1-3.

The walls of wood cells consist of various layers, which differ in structure and chemical composition. The individual cells of wood tissue are glued together in the middle lamella (which consists mainly of lignin, polyoses, and pectins). Often, there is no precise visible border between the pure middle lamella and the outer cell wall layer (the primary wall), which is formed by a net-like arrangement of cellulose fibrils embedded in a matrix of lignin and polyoses. The middle lamella and primary walls are often called the "compounded middle lamella" (IARC 1995).

The next layer is the secondary wall, which is further subdivided into secondary walls 1 (S1) and 2 (S2). S1 and S2 contain densely packed cellulose fibrils arranged in parallel. In S1, the fibrils run at a wide angle in relation to the fiber axis, whereas in S2, they run at a small angle. S2 is the thickest wall layer, accounting for 50% to 90% of the cell wall (IARC 1995).

At the inner border of the cell wall, there is a final layer (the tertiary wall), in which the cellulose fibrils run at an angle similar to that of S1. The lignin content decreases from the compounded middle lamella through S2, while the cellulose content increases in the

same direction. The organic matter of wood (extractives) is found in the resin canals and parenchymal cells (IARC 1995).

Table 1-3. Comparison of softwood and hardwood characteristics

Characteristic	Gymnosperms (conifers, or softwoods)	Angiosperms (deciduous trees, or hardwoods)
World production of industrial roundwood (1980) (× 1000 m^3)	990,000	450,000
Density, mean and range (g/cm^3)	white (silver) fir: 0.41 (0.32–0.71) European spruce: 0.43 (0.30–0.64) Scotch pine: 0.49 (0.30–0.86)	European beech: 0.68 (0.49–0.88) European oak: 0.65 (0.39–0.93)
Fibers	long (1.4–4.4 mm)	short (0.2–2.4 mm)
Cell type	one (tracheids)	various
Cellulose	~40% to 50%	~40% to 50%
Unit	β-D-glucose	β-D-glucose
Fiber pulp	long	short
Polysoses	~15% to 30%	~25% to 35%
Units	more mannose, more galactose	more xylose
Lignin	~25% to 35%	~20% to 30%
Units	mainly guaiacyl	mainly syringyl or guaiacyl
Methoxy group content	~15%	~20%
Extractives content		
Nonpolar (e.g., terpenes)	high	low
Polar (e.g., tannins)	low	high

Source: Fengel and Wegener 1989, cited in IARC 1995

2 Human Exposure

2.1 Use

Wood dust has limited commercial uses, but wood is one of the world's most important renewable resources. It is estimated that forests cover more than one-third of the world's total land area, with a total biomass of one trillion cubic meters, of which around 3.5 billion cubic meters are harvested annually. "Industrial roundwood" refers to categories of wood not used for fuel, which include sawn wood (54%), pulpwood (21%), poles, pit props (14%), and wood used for other purposes, such as particle board and fiberboard (11%) (IARC 1995).

Wood dust is used to prepare charcoal, as an absorbent for nitroglycerin, as a filler in plastics, and in linoleum and paperboard (Radian 1991). Another commercial use for wood dust is in wood composts (Weber *et al.* 1993).

2.2 Production

Wood dust is created when machines or tools are used to cut or shape wood materials. Industries where high amounts of wood dust are produced include sawmills, dimension mills, furniture industries, cabinetmaking, and carpentry (IARC 1995).

Total estimated production values for wood used in industry in the United States for 1990 was 311.9 million cubic meters softwood and 115 million cubic meters of hardwood (Demers *et al.* 1997).

2.3 Analysis

Wood dust usually is measured as airborne dust concentrations, by particle size distribution, by type of wood, and by other characteristics of wood (IARC 1995). Backlighting with a dust lamp, or Tyndall beam, is useful for identifying sources of dust emission (Hamill *et al.* 1991).

2.3.1 Airborne dust concentrations

Total airborne dust concentrations are characterized as mass per unit volume (usually milligrams per cubic meter). The general method of collection is a standard gravimetric method that involves the use of a sampling pump to collect a known volume of air through a special membrane filter contained in a plastic cassette. The detection limit for personal sampling of wood dust is about 0.1 mg/m^3. Polyvinyl chloride filters are preferred, because of the highly variable water content of wood dusts (IARC 1995).

Airborne dust is collected on polyvinyl chloride filter media through the use of portable sampling pumps with inlets for respirable and inspirable particles. Respirable dust is sampled through a 10-mm nylon cyclone (centrifugal separator) that is designed to accept 50% of unit density spherical particles of 3.5-μm aerodynamic diameter. Inspirable (inhalable) dust includes large particles that may deposit in the respiratory system. Samplers that measure inspirable wood dust concentrations must maintain a sampling efficiency of > 50% for particles up to 100-μm aerodynamic diameter (IARC 1995, Weber *et al.* 1993).

The NIOSH sampling method (NIOSH Method 0500) for total airborne dust consists of collecting dusts on tares 37-mm hydrophobic filters (PVC, 2 to 5 μm pore size or equivalent). Sampling rates of 1-2 L/min are recommended with a recommended filter maximum dust loading of 2 mg of total dusts. Dust weights are determined using a microbalance capable of weighing to 0.001 mg and dust concentrations are expressed as mg/m^3 of total dust (NIOSH 1994).

Particle size-selective sampling methods have been proposed by several organizations including the American Conference of Governmental Industrial Hygienists (ACGIH) and the International Standards Organization. For wood dusts, the appropriate exposure measure is the inspirable or inhalable mass which is defined as those materials that are deposited anywhere in the respiratory tract. The ACGIH has defined the sampling characteristics of inhalable mass samplers to have a sampling efficiency of 50% for particles of 100 μm aerodynamic diameter. Sampling devices which meet these criteria have been developed and used for sampling wood dusts (Phalen *et al.* 1986, Mark and Vincent 1986, Hinds 1988, and Vaughan *et al*. 1990).

2.3.2 Particle size distribution

Particle size distribution is determined with a multistage cascade impactor. The impactor separates the particles by mass, allowing dust collected at various stages to be weighed and a particle size (mass) distribution to be determined. Wood dust samples also can be analyzed by optical microscopy that classifies particles by equivalent circular diameters. A particle-size frequency distribution can then be determined (IARC 1995).

2.3.3 Wood type

Wood type is frequently classified by wood species, as hardwood or softwood. "Hardwood" refers to broadleaved trees, or angiosperms, and "softwood" refers to conifers, or gymnosperms. Although the majority of trees harvested worldwide are hardwoods (58% of volume), much of the hardwood is used for fuel. For industrial purposes, softwood is the major wood used (69%), although this can vary from region to region (IARC 1995).

2.3.4 Other characteristics of wood

Several other characteristics of wood sometimes are reported. Irregular shapes of wood dust particles can be recorded in photomicrographs or by scanning electron microscopy. Chemical substances that occur naturally or have been added to wood are sometimes described. There is no standard procedure, however, for measuring the extractable fraction in wood dust (IARC 1995).

2.4 Environmental occurrence

Wood dust occurs in the environment in areas where machinery or tools are used to cut or shape wood. The literature provided no information about ambient concentrations of wood dust.

2.5 Environmental fate

No flash-point data are available for wood dust. However, wood dust is flammable and will ignite in the environment. It may present a strong to severe explosion hazard if a dust cloud contacts an ignition source. Wood dust is stable under normal laboratory conditions. The literature provided no information about decomposition in the environment (Radian 1991).

2.6 Environmental exposure

2.6.1 Sanders

Exposure to wood dust occurs when individuals use machinery or tools to cut or shape wood. Deposition within the airways depends on the size, shape, and density of the dust particles and the turbulence and velocity of the airflow (IARC 1981). Particles with a diameter > 5 µm are deposited almost completely in the nose. Respirable particles (0.5 µm to 5 µm) are those deposited in the lower airways (IARC 1981, 1995). Use of hand held electric sanders has been identified as a particularly dusty process, which would lead to exposure to dust. Wood dust concentrations vary with type of dust extraction, amount of wood removed, and type of sander (Thorpe and Brown 1994). For electrical orbital sanders without integral dust extraction, total inhalable or inspirable dust concentrations ranged from 0.42 to 8.01 mg/m^3; dust concentrations were reduced 84.3% to 97.97% when the sanders were used with fitted bags. For electric belt sanders, total inhalable dust concentrations ranged from 10.2 to 19.8 mg/m^3 without integral dust extraction and were reduced 66.1% to 93.5% with bags. For electrical orbital sanders with external dust extraction, total dust concentrations ranged from 0.022 to 0.739 mg/m^3, and respirable dust concentrations ranged from 0.003 to 0.291 mg/m^3. For electric belt sanders, total dust concentrations ranged from 0.27 to 3.740 mg/m^3, and respirable dust concentrations ranged from 0.003 to 0.936 mg/m^3. Rotary sanders with external dust extraction produced total dust concentrations ranging from 0.002 to 0.699 mg/m^3, and respirable dust concentrations ranged from 0.001 to 0.088 mg/m^3.

2.6.2 Compost containing wood dust

Environmental exposure to wood dust also occurs through handling of compost containing wood dust. Wood compost materials consist of successive layers of chopped leaves, bark, and wood stored outdoors during spring where high rainfall is expected. Visible clouds of fine particulates are easily generated when the compost materials are agitated. Routine exposures were determined with samplers at breathing zone-level during loading and unloading of compost. The worst-case exposures were collected directly from the visible clouds generated by compost agitation. Background concentrations were obtained from samplers upwind from the compost pile (Weber *et al.* 1993). Respirable dust concentrations during compost handling were measured with portable sampling pumps operated at 1.7 L/min and designed to accept 50% of unit density spherical particles of 3.5-µm aerodynamic diameter. Inspirable (inhalable) dust concentrations were measured with portable sampling pumps operated at 2.0 L/min. Table 2-1 summarizes the inspirable and respirable dust concentrations that were measured to determine total dust concentrations in air during compost handling.

Table 2-1. Inspirable and respirable dust concentrations in air during compost handling

Exposure	Sampling time (min)	Inspirable[a] dust (mg/m^3)	Respirable[b] dust (mg/m^3)
Routine	141	0.74	0.42
Worst-case	20	149	83
Background	232	0.32	–

Source: Weber *et al.* 1993
[a]Dust particles that can be inhaled.
[b]Dust particles from 0.5 µm to 5 µm in diameter.

2.7 Occupational exposure

The National Occupational Exposure Survey, conducted from 1981 to 1983, estimated that around 600,000 workers were exposed to wood dust in the United States. Forestry workers were not considered exposed in this survey; according to the Food and Agriculture Organization of the United Nations, there were 400,000 forestry workers in 1990 (IARC 1995, Noertjojo *et al.* 1996).

Teschke *et al.* (1999) analyzed 1,632 measurements of personal time-weighted-average (TWA) airborne wood dust concentrations in 609 establishments on 634 inspection visits that were reported to OSHA's Integrated Management Information System between 1979 and 1997. Exposures ranged from 0.003 to 604 mg/m^3, with an arithmetic mean of 7.93 mg/m^3 and a geometric mean of 1.86 mg/m^3. Exposure levels have decreased significantly over time (the unadjusted geometric mean was 4.59 mg/m^3 in 1979 and 0.14 mg/m^3 in 1997). Table 2-2 summarizes wood dust exposure measurements for all types of wood and for specific wood dust substance codes.

Table 2-2. Personal TWA wood dust exposure concentrations

Type of wood	N	Arith. mean (mg/m^3)	Geomet. mean (mg/m^3)	Geomet. SD (mg/m^3)	% < limit of detection	Max. (mg/m^3)
All types	1,632	7.93	1.86	6.82	3.6	604
Hardwood	920	7.73	2.31	5.88	2.4	286
Softwood	455	9.13	1.71	6.95	3.5	604
Western red cedar[a]	18	23.1	1.00	14.2	11.1	334
All except western red cedar[b]	239	5.29	1.01	9.14	7.5	122

Source: Teschke *et al.* 1999
[a]Measurements reported only in 1990, 1991, 1992, and 1996.
[b]Measurements reported only in 1989 through 1997.

Table 2-3 lists summary statistics for each industry group and each job group within industries that had at least 10 measurements. Jobs with high exposure to wood dust included sanders in the transportation equipment industry (unadjusted geometric mean = 17.5 mg/m^3), press operators in the wood products industry (12.3 mg/m^3), lathe operators in the furniture industry (7.46 mg/m^3), and sanders in the wood cabinet industry (5.83 mg/m^3). Industries with high geometric means included chemical and petroleum products and rubber and plastics products, in which exposures occurred in sanding, pattern-making, and mill and saw operation. Industries with the lowest exposures included industrial patterns, paper and paperboard mills, schools and institutional training facilities, and veneer and plywood mills.

Table 2-3. Wood dust exposure concentrations for industry and job groups

Industry or job group	N	Arith. mean (mg/m^3)	Geomet. mean (mg/m^3)	Geomet. SD	Min. (mg/m^3)	Max. (mg/m^3)
Wood-related industries						
Carpentry and floor laying	10	8.62	1.83	9.30	< 0.02	58.8
Sawmills	228	4.13	1.11	5.97	< 0.02	54.9
Saw operator, head	14	5.19	1.98	5.44	0.08	16.8
Saw operator, edger	17	3.42	1.41	1.06	0.04	26.3
Offbearer/sorter	17	3.03	1.21	4.59	0.09	13.3
Saw operator, cut-off	10	1.92	0.82	4.19	0.11	9.92
Machine operator, nec	16	2.01	0.80	5.00	< 0.02	12.3
Saw operator, trim	16	1.09	0.73	2.31	0.19	6.23
Millwork	133	4.54	1.02	6.85	< 0.02	93.3
Sander, nec	17	7.06	1.45	10.72	0.02	28.7
Machine operator, nec	12	3.09	0.54	8.27	0.05	18.7
Wood cabinets	144	10.8	4.19	5.16	< 0.02	119
Sander, nec	50	13.2	5.83	5.19	< 0.02	83.6
Saw operator, nec	15	20.7	3.23	11.0	< 0.02	119
Veneer and plywood mills	40	3.11	0.63	7.34	< 0.02	43.0
Wood containers	20	21.0	1.51	16.8	< 0.02	316
Wood pallets and skids	36	3.56	1.31	5.14	< 0.02	21.9
Saw operator, nec	12	2.3	0.74	7.19	< 0.02	7.72
Wood buildings and mobile homes	17	5.50	2.41	4.97	0.09	18.5
Reconstituted wood products	21	6.64	1.49	7.79	< 0.02	55.5
Wood products, nec	127	12.2	3.41	4.94	< 0.02	334
Press operator	11	25.0	12.3	4.12	0.50	87.8
Sander, nec	24	11.0	3.92	3.49	0.26	155
Machine operator, nec	10	7.08	2.35	3.88	0.35	49.1
Saw operator, nec	15	6.85	0.94	8.61	< 0.02	54.1
Furniture	496	7.22	2.39	5.79	< 0.02	286
Lathe operator	11	33.1	7.46	4.56	1.43	286
Sander, nec	127	10.5	3.96	4.96	< 0.02	131
Cabinet maker	21	5.74	3.72	2.92	0.30	15.0

Industry or job group	N	Arith. mean (mg/m^3)	Geomet. mean (mg/m^3)	Geomet. SD	Min. (mg/m^3)	Max. (mg/m^3)
Sander, hand	23	7.88	3.59	3.75	0.14	65.4
Wood worker	20	10.0	3.51	4.32	0.50	58.4
Router operator	13	5.66	3.12	3.02	0.48	28.3
Laborer	14	4.54	2.14	3.52	0.20	30.0
Machine operator, nec	32	5.20	2.05	4.91	< 0.02	34.9
Saw operator, nec	26	4.21	1.97	4.55	< 0.02	27.7
Sander, belt	12	7.67	1.79	8.99	0.04	38.3
Sander, stroke	10	2.67	1.71	3.57	0.08	6.82
Miscellaneous jobs	21	3.80	1.10	8.25	< 0.02	17.1
Assembler	14	3.78	0.86	13.2	< 0.02	13.1
Saw operator, rip	11	0.71	0.33	5.38	< 0.02	1.61
Paper/paperboard mills	23	2.15	0.77	4.71	0.06	14.9
Industrial patterns (pattern maker)	17	2.31	0.99	3.79	0.15	17.1
Woodworking machinery	13	7.26	2.23	6.69	0.03	49.3
Lumber and building materials	18	6.02	1.77	6.30	< 0.02	40.0
Other industries[a]						
Construction and maintenance	23	25.7	1.21	10.5	< 0.02	538
Carpenter	12	47.3	2.33	9.71	0.05	538
Chemical and petroleum products: sander, mill and saw operators	11	61.3	7.48	5.42	1.00	604
Rubber and plastic products: press operators, pattern makers, sanders	21	30.0	8.86	8.47	0.15	173
Foundries and smelters: pattern makers, carpenters	13	4.00	1.46	6.57	< 0.02	21.5
Fabricated metal products: router, mill and saw operators	19	11.8	3.17	5.77	0.16	90.1
Electric equipment: box workers, carpenters, router operators, and shapers	16	4.35	1.44	7.86	0.04	12.4
Transportation equipment	39	7.21	1.94	6.41	0.05	41.7

Industry or job group	N	Arith. mean (mg/m^3)	Geomet. mean (mg/m^3)	Geomet. SD	Min. (mg/m^3)	Max. (mg/m^3)
Sander, nec	10	20.3	17.5	1.79	5.90	41.7
Ship/boat building and repair: carpenters, saw operators, and sanders	22	6.38	2.63	5.08	0.10	35.3
Musical instruments: sanders	11	4.73	3.45	2.60	0.40	10.2
Miscellaneous manufacturing: sanders, woodworkers, lathe and saw operators	43	12.0	3.74	6.50	0.03	122
School/institutional training	39	3.51	0.36	13.2	<0.02	32.6
Vocational instructor	18	0.72	0.10	10.3	<0.02	4.25

Source: Teschke *et al.* 1999
[a]Most frequent jobs listed, where no single job had at least 10 measurements.

Teschke *et al.* (1999) used a multiple regression model to predict wood dust exposure levels by such factors as year, state, job, and industry. Values predicted by the model fell in the range of 0.015 to 36.0 mg/m^3, with a geometric mean of 1.85 ± 2.95 mg/m^3. Tables 2-4 and 2-5 list predicted mean exposure levels calculated from the model parameter estimates for industry groups and job groups.

Table 2-4. Geometric mean wood dust concentrations for industry groups, unadjusted

Industry group	Unadjusted geometric mean (mg/m^3)	N
Chemical and petroleum products	7.28	11
Rubber and plastic products	8.86	21
Wood cabinets	4.19	144
Industrial patterns	0.99	17
Foundries/smelters	1.46	19
Wood products, nec	3.41	127
Woodworking machinery	2.23	13
Musical instruments	3.45	11
Ship/boat building	2.63	22
Fabricated metal products	3.18	19
Furniture	2.40	496

Miscellaneous manufacturing	3.75	43
Carpentry and floor laying	1.83	10
Wood buildings and mobile homes	2.41	17
Reconstituted wood products	1.49	21
Transportation equipment	1.94	39
Lumber and building materials	1.77	18
Wood pallets and skids	1.31	36
Millwork	1.02	133
Electronic equipment	1.44	16
Wood containers, nec	1.51	20
Construction and maintenance	1.22	23
Sawmills	1.11	228
Veneer and plywood	0.63	40
Paper/paperboard mills	0.77	23
School/institutional training	0.36	39

Source: Teschke *et al.* 1999

Table 2-5. Geometric mean wood dust concentrations for job groups, unadjusted

Job group	Unadjusted geometric mean (mg/m^3)	N
Sander, finish	7.19	14
Lathe operator	4.29	21
Finisher	4.16	21
Press operator	8.65	23
Tenoner operator	3.47	12
Sander, nec	3.69	281
Shaper	3.96	19
Saw operator, band saw	1.63	20
Sander, hand	3.65	42
Inspector/grader	1.80	17
Saw operator, head saw	1.97	16
Heavy equipment operator	0.67	11
Router equipment	4.55	35
Saw operator, table saw	1.97	16
Heavy equipment operator	0.67	11
Clean up	0.83	14
Sander, belt	2.47	26
Laborer	2.13	37
Mill operator	1.43	19
Cabinet maker	2.06	35
Planer operator	1.20	15
Feeder	1.93	12
Wood worker	1.92	73
Carpenter	1.62	61
Miscellaneous jobs	1.46	102
Foreman	1.51	17
Saw operator, cut-off	0.99	15
Shipper operator	1.02	17
Machine operator, nec	1.29	90
Sander, stroke	1.71	10
Saw operator, gang saw	1.45	11
Saw operator, rip saw	1.01	24

Job group	Unadjusted geometric mean (mg/m^3)	N
Edger	1.02	20
Supervisor/manager	1.09	10
Saw operator, trim saw	0.79	20
Off bearer/sorter	0.86	37
Saw operator, nec	0.97	113
Assembler	0.88	22
Saw operator, chop saw	0.53	15
Vocational instructor	0.10	18
Pattern maker	0.79	33

Source: Teschke *et al.* 1999

Several researchers have reported particle size distributions for wood dust in workplace air in various industries (summarized in Table 2-6). Some studies reported that the particle size distribution varied according to the woodworking operation, with sanding producing smaller particles than sawing (Hounam and Williams 1974, Darcy 1984, Liu *et al.* 1985, all cited in IARC 1995), but others found no consistent differences (Holliday *et al.* 1986, Lehmann and Frolich 1988, and Pisaniello *et al.* 1991, all cited in IARC 1995). The majority of the wood dust mass was reported to be contributed by particles larger than 10 μm in aerodynamic diameter (Whitehead *et al.* 1981, Darcy 1984, Lehmann and Frohlich 1987, 1988, Hinds 1988, and Pisaniello *et al.* 1991, all cited in IARC 1995). Holliday *et al.* (1986, cited in IARC 1995) found that 61% to 65% of the particles measured between 1 and 5 μm in diameter.

Table 2-6. Particle size distribution of hardwood dust (% by mass)

Wood, operation	Total dust (mg/m^3)	Stage[a] 0	1	2	3	4	5	6	7	Back-up filter
Oak, hand sanding	6.9	72.6	9.6	5.1	3.3	2.3	1.7	1.7	1.5	2.2
Oak, machine sanding	2.7	65.0	12.2	3.9	4.2	3.0	3.4	3.0	2.1	3.3
Oak, sanding (hand portable machine)	2.7	47.2	14.6	7.2	9.1	7.0	4.8	2.6	2.3	5.2
Oak and beech, sawing and machine sanding	5.4	44.4	21.9	7.0	7.2	2.9	2.4	1.1	2.4	10.7
Particle board and beech, sawing and planing	9.4	65.1	15.9	6.1	8.2	2.8	0.9	0.5	0.5	0.0
Ash, hand sawing	1.9	49.5	16.7	14.3	10.1	4.3	2.2	1.2	0.0	1.7
Beech, sawing	4.1	62.7	12.7	9.5	3.5	2.9	2.8	2.4	1.9	1.6

Source Lehmann and Frohlich 1988, cited in IARC 1995

[a]Stage 0, > 9.0 μm; stage 1, 5.8–9.0 μm; stage 2, 4.7–5.8 μm; stage 3, 3.3–4.7 μm; stage 4, 2.1–3.3; stage 5, 1.1–2.1 μm; stage 6, 0.65–1.1 μm; stage 7, 0.43–0.65 μm.

2.8 Biological indices of exposure

Exposure to many types of wood dust can give rise to asthma. In observations of workers exposed to wood dust in a furniture plant, nonsmoking workers had higher prevalence rates of cough, phlegm, and wheeze than control subjects derived from a population sample. An observed decrease in forced expiratory volume in the first second suggests that both hardwood and softwood dust exposure are associated with airflow obstruction (Noertjojo *et al.* 1996).

In other studies, healthy subjects exposed to wood dust in a sawmill showed a slight inflammatory reaction. The median concentration of interleukin 6 in the nasal lavage fluid increased after exposure to wood dust from 0.5 to 5.9 pg/mL in subjects without particle filters ($P < 0.05$). Interleukin 6 was used as a marker for the release of inflammatory cytokines and thus for airway inflammation (Dahlqvist *et al.* 1996).

Tannins are found in all woods as well as in most other dusts of plant origin. Hardwoods generally contain more tannins than softwoods. Measurement of airborne tannin concentrations has been proposed as an indicator of hardwood exposure, although this method has not bee applied broadly (Bhattacharjee *et al.* 1979).

2.9 Regulations

The OSHA regulates wood dust under the Occupational Safety and Health Act of 1970 and the Construction Safety Act. Personal protective equipment is required for working with any process that might produce wood dust, including the use of hand and power tools. The Act states that a collecting system is required for sawmills that produce wood dust. The OSHA established a permissible exposure limit (PEL) of 15 mg/m^3 of air for the total dust and 5 mg/m^3 for the respirable fraction of wood dust, all softwoods and hardwoods, except western red cedar (as a nuisance dust). OSHA also regulates all other dust under "particulates not otherwise regulated" with a PEL of 15 mg/m^3 for total dust and 5 mg/m^3 for respirable dust. .

The National Institute for Occupational Safety and Health established a recommended exposure limit of 1 mg/m^3 for dust from all wood except western red cedar, as a TWA for up to a 10-hour workday and a 40-hour workweek. The American Conference of Governmental Industrial Hygienists assigned threshold limit values of 1 mg/m^3 for certain hardwoods, such as beech and oak, and 5 mg/m^3 for softwoods except western red cedar, as TWAs for a normal 8-hour workday and a 40-hour workweek. It also established a short-term exposure limit (STEL) of 10 mg/m^3 for softwood, for periods not to exceed 15 minutes. Exposures at the STEL concentration should not be repeated more than four times a day and should be separated by intervals of at least 60 minutes. OSHA regulations dealing with wood dust are summarized in Table 2-7.

Table 2-7. OSHA regulations

Regulatory action	Effect of regulation and other comments
29 CFR 1910.132—SUBPART I—Personal Protective Equipment. Promulgated: 62 FR 111, 6/96. U.S. Codes: 29 U.S.C. 653, 655, 657, 5 U.S.C. 553.	Spectacles with side protection, goggles, or face shields are required when chipping, woodworking, sawing, drilling, chiseling, or powered fastening, to protect from flying fragments, objects, large chips, particles, sand, and dirt.
29 CFR 1910.261—SUBPART R—Special Industries. Promulgated: 62 FR 111, 6/96. U.S. Codes: 29 U.S.C. 653, 655, 657. Sawmills	All mills containing one or more machines that create dust, shavings, chips, or slivers during a period of time equal to or greater than one-fourth of the working day shall be equipped with a collecting system. It may be either continuous or automatic, and shall be of sufficient strength and capacity to enable it to remove such refuse from points of operation and immediate vicinities of machines and work areas.
29 CFR 1910.1000 Air Contaminants Table Z-1 Limits for Air Contaminants. Promulgated: 62 FR 42018, 08/04/97.	The PEL limit for particulates not otherwise regulated is 15 mg/m^3 for total dust and 5 mg/m^3 for resiparable dust.
29 CFR 1910.1000 TABLE Z-3 Mineral Dusts. Promulgated: 54 FR 2920, 01/19/89, 54 FR 28059, 07/05/89.	The PEL TWA is 15 mg/m^3 total dust and 5 mg/m^3 for respirable dust.
29 CFR 1926.300—SUBPART I—Tools-Hand and Power. Promulgated: 55 FR 9033, 1/90. U.S. Codes: 40 U.S.C. 333, 29 U.S.C. 653, 655, and 657.	Employees using hand and power tools and exposed to the hazard of falling, flying, abrasive, and splashing objects or exposed to harmful dusts, fumes, mists, vapors, or gases shall be provided with the particular personal protective equipment necessary to protect them from the hazard.

Source: The regulations in this table have been updated through the 1999 Code of Federal Regulations 29 CFR, 1 July 1999.

3 Human Cancer Studies

The literature on wood dust exposure and cancer in human populations was reviewed by the IARC in 1995, when it classified wood dust as *carcinogenic to humans* (Group 1). Two reviews also were published in 1995 that reanalyzed either case-control studies (Demers *et al*. 1995a) or cohort studies (Demers *et al.* 1995b) by calculating summary risk estimates for the pooled data from the studies. Most of the human studies used for these analyses were reviewed individually by the IARC (1995). The IARC reviewed an "in press" copy of the pooled analysis of twelve case-control studies (Demers *et al*. 1995a) and discussed the findings in its 1995 monograph. However, the pooled reanalysis of five cohort studies (Demers *et al.* 1995b) was not available for the IARC review. The IARC review and the two Demers *et al.* (1995a,b) reviews are summarized in Section 3.1. Relevant case-control studies published after the 1995 IARC review are then summarized, and their contributions to current understanding of the link between wood dust and cancer are assessed.

3.1 IARC evaluation and 1995 reanalyses of epidemiologic studies

In 1981 and 1987, IARC monographs addressed the relationship between employment in wood industries and cancer. The IARC (1987) concluded that furniture making and cabinetmaking were associated with increased risk of cancer. Evidence suggesting increased risk of cancer in lumber and pulp and paper industries and for carpentry and joinery also were cited. Wood dust was cited as one potential exposure linking all these industries. The potential link between wood dust and cancer was addressed in a subsequent monograph (IARC 1995). Strong and consistent associations with cancer of the nose (nasal cavities and paranasal sinuses) were noted both for occupations associated with wood dust exposure and for directly estimated wood dust exposure. The evidence included nine case reports, 25 case-control studies, and seven cohort-based analyses specifically addressing nasal cancer.

The cohort studies were of occupational cohorts: four of furniture makers (U.K., Denmark, U.S., and Germany), one of sawmill workers, one of plywood workers, and one of wood-related occupations. Most of these studies reported exposure by occupational title, but one study (U.K.) addressed the issue of exposure to wood dust. Excesses of nasal cancer mortality were reported for the furniture-maker cohorts from Denmark (standardized mortality ratio [SMR] = 4.7, 95% CI = 2.5 to 6.8, 4 deaths) and the United Kingdom (SMR = 8.2, 95% CI = 3.7 to 16, 9 deaths) and the wood-related occupations cohort (SMR = 2.0, 2 deaths). Three of the other cohort studies may have lacked the ability to detect rare cancers (such as nasal cancer) because of their small size.

Demers *et al*. (1995b) conducted a pooled analysis of five cohorts of workers in wood-related industries. The combined cohort consisted of 28,704 persons from two furniture worker cohorts (U.K. and U.S.), two U.S. plywood-worker cohorts (one of which was reviewed by the IARC), and a cohort of wood model makers. Significant excess mortality from nasal cancer (SMR = 3.1, 95% CI = 1.6 to 5.6, 11 cases) and nasopharyngeal cancer (SMR = 2.4, 95% CI = 1.1 to 4.5, 9 cases) was observed. The overall excess for nasal cancer was due to an excess among the British furniture workers cohort. Exposure was

stratified according to the probability of being exposed (possible, probable, and definite), decade of first exposure, and duration of exposure. The risks for both sinonasal and nasopharyngeal cancer were highest in individuals classified as having had definite exposure, exposure before 1940, and exposure of the longest duration (greater than 29 years).

These findings from the cohort studies were strongly corroborated by the case-control studies, most of which reported significant risks for nasal cancer either due to exposure to wood dust or for specific wood-related occupations. Several studies reported exposure-response relationships. Risks were highest for adenocarcinoma, with a few European studies reporting very high relative risks (greater than 50) for specific occupations (furniture making), for specific categories of wood (mainly hardwood), or in the high-exposure strata. Elevated risks also were observed in U.S. studies; however, the magnitudes of the risk estimates were lower. The relative contributions of softwood and hardwood to risk were unclear, because few studies isolated softwood exposure; however, there were indications that softwood was a weaker risk factor (see Section 5 for possible differences in genotoxicity between hardwoods and softwoods and Section 6 for tannin concentrations in hardwoods and softwoods). Studies of squamous-cell carcinoma of the nasal cavities and paranasal sinuses gave less consistent results and reported smaller risks than for adenocarcinoma. Woodworkers in Japan were reported to be affected only by squamous-cell carcinoma (Nylander and Dement 1993).

A pooled analysis of 12 case-control studies showed a high risk of adenocarcinoma among men employed in wood-related fields (odds ratio [OR] =13.5, 95 % CI = 9.0 to 20). Regarding specific job categories, elevated risks in men were observed for sawmills, manufacturing of furniture and other wood products, and carpentry. The risk of adenocarcinoma was greatest among men with the highest exposure (OR = 45.5, 95% CI = 28.3 to 72) and increased with duration of exposure. Women in wood-related occupations also appeared to have an elevated risk of adenocarcinoma (OR = 2.5, 95% CI = 0.5 to 12) and squamous cell carcinoma (OR = 2.1, 95% CI = 0.8 to 5.5); the risk of the latter increased with duration of exposure. However, these estimates were based on small numbers of cases in exposed workers (two adenocarcinomas and six squamous-cell carcinomas). The risk of squamous-cell carcinoma was not associated with wood dust exposure in men (OR = 0.8) except for those employed for 30 years in jobs with exposure to fresh wood (OR = 2.4, 95% CI = 1.1 to 5.0).

The association of wood dust with elevated cancer risk in so many different kinds of jobs in so many countries strongly suggests that the elevated risk was due wholly or in part to wood dust itself, rather than concurrent exposure(s) to other substances, such as formaldehyde. This argument is bolstered by the magnitude of the observed associations, which exceeded those seen with other chemical exposures.

Many case-control studies showed indications of an association between wood dust and cancer of the nasopharynx or larynx. For nasopharyngeal cancer, eight of nine studies had odds ratios of at least 1.3, with three reaching statistical significance. For laryngeal cancer, nine of ten studies had elevated odds ratios, one of which was significant. Lack of support from the individual cohort studies and the possibility of confounding by other

factors led to the conclusion that, while the evidence was suggestive, it was not conclusive. Nevertheless, the pooled cohort analysis found an excess of nasopharyngeal cancer (Demers *et al*. 1995b).

Evidence of association between wood dust or wood-related occupations and Hodgkin's disease was provided by case-control but not cohort studies. The pooled cohort analysis provided some support for an excess of lymphatic and hematopoietic neoplasms, particularly multiple myeloma (SMR = 2.0, 95% C I= 0.5 to 5.1) (Demers *et al.* 1995b). The risk of multiple myeloma increased with the probability of assumed exposure to wood dust. However, multiple myeloma may be related to possible chemical exposures in wood-related industries.

Several studies reported an increased risk of colorectal cancer among wooden pattern model makers exposed to wood dust in the automobile industry; however, these studies were criticized as having methodological problems. The epidemiologic evidence for cancer at other anatomical sites was judged too inconsistent to allow conclusions about the role of wood dust.

In its final evaluation, the IARC concluded that there was sufficient evidence for the carcinogenicity of wood dust in humans and classified it as *carcinogenic to humans* (Group 1).

3.2 Recent studies of wood dust

The literature on cancer and exposure to wood dust or related occupations published since IARC (1995) includes five cohort and eleven case-control studies. The results of each study are described below, organized by study design. Recent cohort and case-control studies are summarized in Tables 3-1 and 3-2, respectively.

3.2.1 Cohort studies of adult cancer

Hansen and Olsen (1995) traced a cohort of 91,182 Danish men diagnosed with cancer between 1970 and 1984. Cancers were identified thorough the national cancer registry and linked to Pension Fund and Central Person and Product Registries to identify each man's company, job title, and potential for formaldehyde and wood dust exposure from 1964 onward. For estimation of risk, the proportion of cancers of a specific type arising among workers exposed to formaldehyde with or without coexposure to wood dust was compared with the proportion arising among unexposed workers. Persons exposed to both formaldehyde and wood dust had higher risks for nasal cancer (standardized proportionate incidence ratio [SPIR] = 5.0, 95% CI = 0.5 to 13.4, 2 cases) and colon cancer (SPIR = 1.8, 95% CI = 0.6 to 3.0, 4 cases) than did persons exposed to formaldehyde alone (for nasal cancer, SPIR = 3.0, 95% CI = 1.4 to 5.7, 9 cases; for colon cancer, SPIR = 1.1, 95% CI = 0.9 to 1.4, 73 cases). No results addressing wood dust exposure alone were presented. This and the small number of persons with both wood dust and formaldehyde exposure make the results difficult to evaluate. There were no associations with cancers at other sites.

Stellman *et al*. (1998) followed 363,823 male participants in the American Cancer Society Cancer Prevention Study from 1982 to 1988. Wood-related occupations showed

an elevated age- and smoking-adjusted relative risk (RR) for all cancers combined (RR = 1.17, 95% CI = 1.05 to 1.30, 381 cases), with particular excesses for cancer of the prostate (RR = 1.49, 95% CI = 1.14 to 1.95, 59 cases) and brain (RR = 2.02, 95% CI = 1.25 to 3.27, 18 cases) and soft-tissue sarcoma (RR = 2.45, 95% CI = 0.97 to 6.17, 5 cases). The elevation in total cancer risk for any wood dust exposure was less marked than that for wood-related occupations (RR = 1.08, 95% CI = 1.01 to 1.15, 961 cases); an excess of prostate cancer persisted (RR = 1.23, 95% CI = 1.00 to 1.50, 110 cases), but the relative risks were much lower for brain cancer (1.14) and sarcoma (0.80). The wood dust exposed group also had a significant excess of lung cancer (RR =1.17, 95% CI = 1.04 to 1.31, 317 cases) and a near-significant excess of stomach cancer (RR = 1.34, 95% CI = 0.96 to 1.87, 40 cases).

Estimated risks for stomach, colon, rectal, and lung cancer and for all cancer combined were consistently elevated for exposure duration of 10 to 19 years vs. < 10 years, but generally showed no further increase for exposure durations of 20 years or more (Stellman *et al*. 1998). Results by duration were not presented for other specific cancers with < 10 cases or that had not been hypothesized *a priori* to be associated with wood dust. Nasal cancer was too rare in the cohort for effective evaluation (one case among the entire dust-exposed group, RR = 1.0). Adjustment for formaldehyde or asbestos exposure did not reduce the risk estimates, but exclusion of persons ill at time of entry into the cohort did. The lack of data on jobs other than the most recent or longest-held one and reliance on self-reported exposure were potential sources of exposure misclassification, and the short follow-up period limited power to detect effects with long latencies. The strengths of this study were the large population and the availability of specific information on smoking habits, asbestos, and formaldehyde exposure.

Langseth and Andersen (1999) studied 4,247 women employed in a Norwegian pulp and paper mill for at least one year between 1920 and 1993, monitoring their cancer incidence from 1953 to 1993. Compared with the national female population, women employed for at least three years in pulp and paper work showed an ovarian cancer standardized incidence ratio (SIR) of 1.6 (95% CI = 1.1 to 2.3, 31 cases), while the SIR for women with less than three years' exposure was 1.2 (95% CI = 0.4 to 2.5, 6 cases). Elevated SIRs were seen for lung and bladder cancer and multiple myeloma in women with less than three years' exposure, but not for longer exposures. No nasal cancer cases occurred in the population. Wood dust exposure was not estimated directly, making dose response hard to evaluate, and the study's small size limited its power for most outcomes.

Andersen *et al*. (1999) followed up 10 million members of the Danish, Norwegian, Finish, and Swedish populations from 1970 through years varying from 1987 to 1991. Cancer mortality was assessed for each of 53 occupational groups, including forestry workers and wood workers. Compared with national rates, overall cancer risk was lower for male forestry workers (SIR = 0.86, 95% CI = 0.84 to 0.88, 6,890 cases) and both male and female wood workers (SIR = 0.93, 95% CI = 0.92 to 0.94, 28,696 cases and SIR = 0.94, 95% CI = 0.88 to 0.99, 1,232 cases). Male, but not female, wood workers showed an elevated risk of nasal cancer (SIR = 1.89, 95% CI = 1.62 to 2.20, 165 cases). Elevated risks were seen for stomach cancer in forestry workers, for pleural cancer in male woodworkers, and for lung cancer in female wood workers, but such elevations were not

seen in other groups. The authors indicated that wood workers and forestry workers probably drank and smoked less than their national-population counterparts, explaining the low risks for many cancers. As no data on all-cause mortality were available, it was unclear whether there was a general "healthy worker" effect in these occupations. The large sample size makes this an important study.

Innos *et al*. (2000) studied 3,723 male and 3,063 female workers employed at two furniture factories in Estonia from 1946 onward, followed through 1995 for incidence of cancer. Workers were classified as having low, medium, or high intensity of exposure. based on employment records. Nasal cancers were twice as common as expected, compared with the national population, but this was based on only three cases (all of which occurred among highly exposed workers). The only significantly elevated risk was for colon cancer (SIR = 1.65, 95% CI = 1.22 to 2.17, 50 cases). Colon cancer risk rose with intensity of exposure among women, but not among men; incorporation of a 20-year latency assumption strengthened the association. The use of total incidence instead of mortality, as well as consideration of intensity of exposure and lag effects, were strengths of this study. However, the sample size limited the ability to detect elevated risks of rarer cancers.

3.2.2 Case-control studies of adult cancer

Wu *et al*. (1995) conducted a case-control study comparing 180 African-Americans and Mexican-Americans with lung cancer, during an unspecified period, with 270 controls drawn from the local population in Texas. Persons reporting occupational exposure to wood dust showed a significantly elevated smoking-adjusted OR for lung cancer (pack-years-adjusted OR = 3.6, 95% CI = 1.4 to 9.1, 23 exposed cases). The same was true for persons with either wood dust exposure or employment in an occupation or industry likely to have involved such exposure (OR = 3.5, 95% CI = 1.4 to 8.6, 30 exposed cases). Mutagen sensitivity, based on counts of chromatid breaks or exchanges (at least one break per cell after bleomycin treatment), was assessed from blood samples. There were significant synergistic effects of wood dust exposure with both mutagen sensitivity and smoking. The OR for mutagen-sensitive individuals exposed to wood dust was 19.7. Compared with non-exposed nonsmokers, smokers unexposed or exposed to wood dust had ORs of 5.9 and 53.9, respectively. Potential bias in control selection seems unlikely, given that education and income were reportedly similar for cases and controls. The statistical strength of these results and the availability of detailed data on smoking habits are offset to some degree by the fact that all individuals with lung cancer who were exposed to wood dust also were smokers. So few nonsmoking subjects (nine controls) were exposed to wood dust that it is unclear from these data whether wood dust exposure has any association with lung cancer in the absence of smoking, with or without mutagen sensitivity.

Fritschi and Siemiatycki (1996) matched 215 non-Hodgkin's lymphoma, 54 Hodgkin's lymphoma, and 23 myeloma cases diagnosed from 1979 to 1985 in Montreal, Canada, with a total of 1,066 randomly selected controls drawn equally from the general population and from individuals with cancer at sites other than the lung. Exposure to wood dust (derived from job history) or employment in the household furniture industry had no association with myeloma or Hodgkin's lymphoma. For non-Hodgkin's

lymphoma, ORs adjusted for age, proxy status, income, and ethnicity, were 0.5 (95% CI = 0.3 to 0.8) for nonsubstantial exposure and 0.8 (95% CI = 0.5 to 1.3) for substantial exposure, versus no exposure. For myeloma and Hodgkin's lymphoma, negative results were not conclusive, because sample sizes were too small.

Teschke *et al*. (1997) compared 54 nasal and 119 bladder cancer cases arising from 1990 to 1992 with controls drawn from the population in British Columbia. For nasal cancer, the age-, gender-, and smoking-adjusted OR for pulp and paper workers was 3.1 (95% CI = 0.4 to 25.4, 3 cases), but the ORs for forestry and sawmill workers were 0.5 (95% CI = 0.1 to 2.4, 2 cases) and 0.4 (95% CI = 0.1 to 1.6, 3 cases). ORs for bladder cancer were 1.5 (2 cases) for pulp and paper workers, 1.6 (15 cases) for forestry workers, and 1.0 (15 cases) for sawmill workers. Control for smoking was a strength of the study, but the small number of nasal cancer cases and lack of control for other occupational exposures limit the utility of the results.

Two studies were based on death certificates. Cocco *et al*. (1998) compared 1,023 gastric cardia cancer deaths with 5,115 noncancer deaths in 24 U.S. states from 1984 to 1992. Although white pulp and paper workers showed an elevated OR (2.0, 95% CI = 1.0 to 3.1, 5 cases), estimated exposure to wood dust across all occupations was not associated with gastric cancer. ORs for low, medium, and high intensity of exposure were 0.8 (95% CI = 0.5 to 1.2), 0.9 (95% CI = 0.4 to 1.8), and 0.9 (95% CI = 0.5 to 1.4), respectively. In a similarly designed study, Cocco *et al*. (1999) compared 41,957 stomach cancer deaths with 83,914 noncancer deaths in 24 U.S. states from 1984 to 1996. A significant association between stomach cancer and wood dust exposure of low intensity was noted among African-American males (OR = 1.16, 95% CI = 1.02 to 1.33, 406 deaths), but no association was seen with medium- or high-intensity exposure (OR = 1.10, 95% CI = 0.93 to 1.32, 206 deaths; OR = 0.80, 95% CI = 0.61 to 1.04, 80 deaths). No statistically significant associations were seen in any other gender or racial group, regardless of exposure intensity. These two studies were limited by reliance on occupational information drawn from death certificates and inability to control for other occupational exposures or potential confounders; however, the large number of cases was a strength.

Gustavsson *et al*. (1998) compared 545 cases of oral, pharyngeal, laryngeal, and esophageal squamous-cell carcinoma with 641 Swedish population controls for the period from 1988 to 1991. For subjects ever exposed to wood dust, the OR for all four sites combined in subjects ever exposed to wood dust was significantly lower than 1.0 (OR = 0.62, 95% CI = 0.43 to 0.90, 69 cases), and ORs were particularly low for pharyngeal cancer (OR = 0.52) and laryngeal cancer (OR = 0.54). Results were controlled for age, alcohol, and smoking, but not other occupational exposures. Although there were no data on intensity or duration of exposure, the authors concluded that exposures were probably relatively low.

Andersson *et al*. (1998) compared 33 lung, 35 stomach, and 10 brain cancer deaths with all other deaths (of a total of 780) occurring from 1960 to 1989 in three parishes surrounding sulfite mills in Sweden. With all "sulfite" and "factory" workers classified as exposed, a significant positive association with exposure was seen for brain cancer, a small and nonsignificant positive association for lung cancer, and a significant inverse

association for stomach cancer. The total number of exposed cases was small for both stomach cancer (4) and brain cancer (5).

Hoppin *et al*. (1999) compared 231 living individuals with histologically confirmed sarcoma with 1,908 randomly selected healthy population controls in eight U.S. states for the period from 1984 to 1988. Subjects were part of the Selected Cancers Study, designed to evaluate potential links between cancer and military service in Vietnam. Elevated ORs for wood dust exposure were found for dermatofibrosarcoma (OR = 1.7, 95% CI = 0.8 to 3.24), leiomyosarcoma (OR = 2.4, 95% CI = 1.4 to 4.2), and skeletal sarcoma (OR = 1.8, 95% CI = 0.9 to 3.3), but not for liposarcoma (OR = 0.6, 95% CI = 0.2 to 1.2) or malignant fibrohistiocytic sarcoma (OR = 0.7, 95% CI = 0.2 to 1.7). The study was one of the few to bring together sufficient sarcomas to evaluate potential associations.

Mirabelli *et al*. (2000) compared living individuals with histologically confirmed nasal cancer (43 cases) and nasopharyngeal cancer (92 cases) with 2,506 controls drawn from the same Selected Cancers Study base population used by Hoppin *et al*. (1999). The percentage of wood or sawdust exposure among nasal cancer patients (25.6%) and nasopharyngeal cancer patients (27.2%) was similar to that among the controls (26.3%). The wood preservative chlorophenol showed a significant association with nasopharyngeal cancer, with an OR of 9.1 (95% CI = 1.4 to 42.9, 3 cases) for substantial exposure ≥ 10 years' duration; however, most chlorophenol exposure occurred among machinists, not wood workers.

Mao *et al*. (2000) studied 1,469 individuals with histologically confirmed non-Hodgkin's lymphoma, age- and gender-matched with 5,073 cancer-free population-based controls from eight Canadian provinces from 1994 to 1997. When ORs were adjusted for age, body mass index, province, and milk consumption, wood dust exposure was not associated with lymphoma in men (OR = 0.9, 95% CI = 0.8 to 1.1, 205 cases). Among women, exposure was associated with lymphoma (OR = 1.4, 95% CI = 1.0 to 2.0, 57 cases), and the OR increased to 1.7 (95% CI = 1.1 to 2.6) for ≥ 7 years of exposure. The authors did not explain why they controlled for milk consumption or how it affected the results, nor did they address the potential effects of coexposures.

Vaughan *et al*. (2000) compared 196 individuals with epithelial nasopharyngeal cancer in four U.S. states with 244 population-based controls. The age, gender, and race-adjusted OR for those ever exposed to wood dust was 1.5 (95% CI = 0.7 to 3.3, 17 cases), but fell to 1.2 (95% CI = 0.5 to 2.7) after adjustment for formaldehyde exposure. Excess incidence of cancer was limited to subjects with moderate exposure (OR = 3.0 for exposure of 2.75 to 15.7 mg/m^3-years) and was not seen among the few subjects with high exposure (OR = 0.4, two cases).

3.3 Discussion

Recent studies of nasal cancer include five cohort and two case-control studies; however, two of the cohorts (Stellman *et al.* 1998, Langseth and Andersen 1999) had no more than one exposed case and thus could not be evaluated. The Scandinavian cohort of Andersen *et al.* (1999) was the only one of sufficient size to contribute reasonable numbers of exposed cases (165 male woodworkers, 19 male forestry workers, and two female

woodworkers), and found a significant elevation of risk in the largest (and probably most highly exposed) group, although not in the two smaller ones. Another cohort study observed elevated risks with wood dust exposure (Innos *et al.* 2000), and the fifth cohort study indicated that addition of wood dust to formaldehyde exposure elevated risk (Hansen and Olsen 1995); however, the latter two studies included few exposed cases. One case-control study (Mirabelli *et al.* 2000) found no association between wood dust exposure and nasal cancer, and the other (Teschke *et al.* 1997) found inconsistent associations across wood-exposed occupations. The strong association for woodworkers in the largest cohort and mixed indications of association in the smaller studies suggest an involvement of wood dust exposure in nasal cancer, consistent with studies reviewed by the IARC (1995).

As noted in the IARC review, the strongest results linking wood dust with nasal cancer came from studies of populations outside the United States, prompting speculation that this might be due to lower exposure levels in U.S. industries, a less carcinogenic mix of wood types in U.S. industries, or both. Of four U.S. studies of cohorts with at least 2,000 workers in occupations associated with wood dust exposure (Stellman and Garfinkel 1984, Robinson *et al*. 1990, Roscoe *et al*. 1992, Miller *et al*. 1994), only one (Stellman and Garfinkel 1984) observed an elevated risk, with two deaths occurring where only one was expected. However, the power of these studies was low; all but one (Miller *et al*. 1994) were so small that no more than one case was expected during the follow-up period. In six U.S. case-control studies (Brinton *et al*. 1977, Roush *et al*. 1980, Brinton *et al*. 1984, Viren and Imbus 1989, Zheng *et al*. 1993, Vaughan and Davis 1991), odds ratios exceeding 1.0 and ranging from 1.3 to 7.5 were found for all wood-exposed occupations examined. Risk was significantly elevated for at least one exposed occupations in four of the studies. In the one study addressing adenocarcinoma specifically (Brinton *et al.* 1984), associations were much stronger for that cancer type, in agreement with the pattern seen in European studies. Thus, although it appears that the excess risk of nasal cancer due to wood dust exposure may be lower for U.S. workers than for their counterparts in other countries, the evidence from the United States is consistent with a carcinogenic effect of wood dust.

Hodgkin's disease showed small positive associations with wood dust exposure or dust-related occupations in three cohort studies (Stellman *et al.* 1998, Andersen *et al.* 1999, Innos *et al.* 2000), but these results were not statistically significant. A case-control study that included Hodgkin's disease (Fritschi and Siemiatycki 1996) reported no relationship with wood dust exposure, although the results for this exposure were not presented. Thus, these later studies provided some weak evidence of association from cohort but not from case-control analyses, the opposite of the pattern seen in the studies reviewed by the IARC. Some evidence exists for a link between wood dust exposure and Hodgkin's disease, but the association is not consistent.

As in the IARC review, risks of laryngeal or nasopharyngeal cancer were elevated in some studies (Stellman *et al.* 1998, Innos *et al.* 2000, Vaughan *et al.* 2000), but not in others (Andersen *et al.* 1999, Mirabelli *et al.* 2000), this association also is inconsistent.

Regarding lung cancer, the case-control study by Wu *et al*. (1995) presented interesting indications of potential synergy between wood dust exposure and both cigarette pack-years and mutagen sensitivity. The lack of any wood-exposed nonsmokers and the restriction of most of the apparent association to one of the two ethnic groups studied leave these results speculative. Associations with lung cancer in cohort studies ranged from significantly positive (Stellman *et al.* 1998, Langseth and Andersen 1999), to significantly positive in women but not in men (Andersen *et al.* 1999), weakly positive only among women (Innos *et al.* 2000), and no association (Hansen and Olsen 1995). Only one of these studies adjusted for smoking (Stellman *et al.* 1998).

The IARC (1995) concluded that the evidence regarding lung cancer was too inconsistent to allow conclusions to be drawn. The evidence included a pooled analysis of five woodworking cohorts (Demers *et al*. 1995b), which found a significant deficit in lung cancer risk (SMR = 0.9, 95% CI = 0.7 to 0.9). However, the cohort analyses did not control for smoking, and other smoking-related conditions, such as buccal and laryngeal cancer and nonmalignant respiratory disease, also showed a deficit, indicating a potential bias due to a lower prevalence of smoking among woodworkers. Of the 24 case-control studies, 17 reported elevated odds ratios, although only 4 were statistically significant. The evidence thus remains inconsistent, but leaves open the possibility that wood dust, independent of or in interaction with tobacco smoking, exerts a modest effect on lung cancer risk.

3.4 Summary

The studies of exposure to wood dust and wood-dust related occupations since the 1995 IARC review provide some evidence that such exposure gives rise to cancer. Most studies failed to adjust for cigarette smoking, alcohol use, diet, or other habits that could modify risk of specific cancers. Many studies lacked sufficient power to detect an association, because the number of exposed cases was small. Specific measurements of wood dust exposure generally were lacking, and most studies based estimates of intensity or cumulative exposure on job categories, often with no data on previous occupations. None of the studies differentiated between the specific types of dust to which subjects were exposed (e.g., hardwood vs. softwood or typical particle size). Most studies also did not address potential exposures to other compounds such as arsenic, formaldehyde, or solvents. However, the probable effect of most of these limitations is nondifferential misclassification or error that would tend to bias results toward the null. Thus, these studies are fully consistent with the IARC (1995) judgment that exposure to wood dust is causally related to human cancer.

Table 3-1 Recent cohort studies of wood dust exposure and cancer

Reference	Population	Exposure	Results	Confounders or comments
Hansen and Olsen 1995	91,182 males with cancer diagnosed 1970–1984, identified through the Danish Cancer Registry, employment history traced 1964–1984 proportion of each cancer among exposed compared with proportion among unexposed	company and job titles from pension records exposed: cabinet makers, joiners, carpenters, any worker employed in wood, furniture, or carpentry industries	SPIR adj. for age and calendar time: formaldehyde + wood dust: nasal 5.0 (0.5–13.4), 2 cases colon 1.8 (0.6–3.0), 4 cases formaldehyde only: nasal 3.0 (1.4–5.7), 9 cases colon 1.1 (0.9–1.4), 73 cases no associations with cancers at other sites	smoking, drinking, diet, socioeconomic, other occupational exposures

Reference	Population	Exposure	Results	Confounders or comments
Stellman *et al*. 1998	363,823 U.S. males enrolled in the American Cancer Society Cancer Prevention Study, followed 1982–1988, including 45,399 woodworkers or wood exposed exposed compared with unexposed	questionnaires exposed: 1) most recent or longest-held job in wood-related occupations (carpentry, woodwork, furniture making or repair, lumber or sawmill) 2) regular exposure to wood dust on the job	RR adj. for age and smoking: wood-related occupations: all cancer 1.17 (1.05–1.30), 381 cases soft-tissue sarcoma 2.45 (0.97–6.17), 5 cases prostate 1.49 (1.14–1.95), 59 cases brain 2.02 (1.25–3.27), 18 cases lung 1.14 (0.94–1.37), 111 cases risk did not approach significance for other sites wood dust exposure: all cancer 1.08 (1.01–1.15), 961 cases soft-tissue sarcoma 0.80 (0.32–2.00), 5 cases prostate 1.23 (1.00–1.50), 110 cases lung 1.17 (1.04–1.31), 317 cases brain 1.14 (0.78–1.64), 32 cases stomach 1.34 (0.96–1.87), 40 cases RR excluding ill at time of entry: lung cancer 1.00 (0.86–1.17) other RRs reduced less dramatically	coexposures, short follow-up, drinking, diet, socioeconomic adj. for formaldehyde or asbestos did not reduce RRs; exclusion of persons ill at entry did

Reference	Population	Exposure	Results	Confounders or comments
Langseth and Andersen 1999	4,247 females employed in a Norwegian pulp and paper mill ≥1 yr during 1920–1993, followed 1953–1993 for cancer incidence compared with national female population	work histories obtained from personnel records exposed: 1) duration of pulp and paper employment (≥ 3 yr vs. < 3 yr) 2) time since first exposure (yr).	age-specific SIR: exposure ≥ 3 yr vs. < 3 yr: ovarian 1.6 (1.1–2.3), 31 cases vs. 1.2 (0.4–2.5), 6 cases nasal or sinus: no exp. cases lung: 1.4 (0.7–2.2), 14 cases vs. 3.0 (1.3–5.9), 8 cases multiple myeloma: 1.1 (0.3–2.8), 4 cases vs. 4.4 (0.9–12.9) 3 cases bladder 0.2 (0.–1.0), 1 case vs. 3.7 (1.0–9.4), 4 cases no significantly increased risks for other sites SIR for ovarian cancer decreased with time since first exposure (results not given for other cancers)	low power for most cancers smoking, drinking, diet, socioeconomic, coexposures

Reference	Population	Exposure	Results	Confounders or comments
Andersen *et al*. 1999	10 million persons in the 1970 Danish, Norwegian, and Finish census or in both the 1970 and 1960 census in Sweden, followed through years varying from 1987 (for Denmark) to 1991 (for Norway) for incident cancer compared with respective national populations	census-reported occupation and industry categorized into 53 occupational groups exposed: 1) forestry workers 2) woodworkers	age-, calendar-period-, and gender-specific SIR: forestry workers (male): all sites 0.86 (0.84–0.88), 6,890 cases nasal 0.85 (0.51–1.33), 19 cases lip 1.35 (1.15–1.58), 152 cases stomach 1.12 (1.04–1.21), 604 cases Hodgkin's 1.22 (0.94–1.55), 66 cases no significantly increased risks for other sites woodworkers (male): all sites 0.93 (0.92–0.94), 28,696 cases nasal 1.89 (1.62–2.20), 165 cases lip 1.15 (1.05–1.26), 486 cases stomach 1.02 (0.98–1.07), 2,072 cases pleura 1.24 (1.06–1.45), 153 cases risk significantly < 1.0 for pharynx, larynx, lung, colon, and 12 other sites woodworkers (female): all sites 0.94 (0.88–0.99), 1,232 cases nasal 0.89 (0.11–3.23), 2 cases lip 1.08 (0.22–3.14), 3 cases lung 1.27 (1.01–1.58), 81 cases pleura 2.14 (0.58–5.47), 4 cases	smoking, drinking, diet, socioeconomic, coexposures

Reference	Population	Exposure	Results	Confounders or comments
Innos *et al*. 2000	3,723 male and 3,063 female workers at two furniture factories in Estonia ≥ 6 mo during 1946–1988, followed through 1995 for incidence of cancer national population used for comparison	work history obtained from records exposed: 1) furniture worker 2) estimated intensity (low, medium, high) 3) duration of wood dust exposure (yr)	nasal cancer: M: 2 obs. vs. 1.07 exp. F: 1 obs. vs. 0.53 exp. all cases among highly exposed gender-, age-, calendar-period-specific SIR: all sites 1.03 (0.95–1.11), 628 cases colon 1.65 (1.22–2.17), 50 cases Hodgkin's 1.53 (0.56–3.32), 6 cases M: risk not consistently inc. with inc. intensity F: colon: high intensity 1.78 (1.02–2.89), 16 cases med. intensity 1.35 (0.58–2.6), 8 cases using 20-year lag, significantly inc. risk with inc. duration for colon and rectal, but not other sites	secondary jobs smoking, alcohol intake, diet, socioeconomic, coexposures

Table 3-2 Recent case-control studies of wood dust exposure and cancer

Reference	Population	Exposure	Results	Confounders and comments
Wu *et al.* 1995	180 histologically confirmed cases of lung cancer among African-American (113) and Mexican-American Texans (67), frequency matched by age, race, and gender with 134 African-American and 136 Mexican-American healthy regional population controls; timeframe not stated	interviews on job and smoking history, blood samples for mutagen sensitivity assays exposed: self-reported: 1) wood-related occupation 2) wood dust exposure 3) wood dust exposure and/or wood-related occupation or industry employment	OR adj. for pack-year, mutagen sensitivity, age, and gender: wood dust 3.6 (1.4–9.1), 23 cases wood-related empl. 2.5 (0.4–16.1), 8 cases any exp. 3.5 (1.4–8.6), 30 cases association strongest for African-Americans, non-small-cell carcinoma: non-small-cell 4.8 (1.2–18.5), 16 cases small-cell 0.7 (0.0–12.4), no exp. cases OR adj. for age, ethnicity, and gender: wood dust + smoking 43.9 (9.5–203.2), 30 cases smoking only 5.9 (3.2–10.9), 127 cases wood dust + mutagen sensitive 19.7 (4.0–96.8), 12 cases	other occupational exposures, no exposed nonsmokers

Reference	Population	Exposure	Results	Confounders and comments
Fritschi and Siemiatycki 1996	217 non-Hodgkin's and 54 Hodgkin's lymphoma plus 23 myeloma cases occurring 1979–1985, matched with randomly selected controls, including 533 population and 533 other cancer	interview for job history probability, duration, and intensity estimated exposed: 1) no vs. non-substantial vs. substantial wood dust exposure 2) household furniture industry worker	OR adj. for age, proxy status, income, and ethnicity: non-Hodgkin's lymphoma vs. no wood dust exposure non-substantial 0.5 (0.3–0.8), 17 cases substantial 0.8 (0.5–1.3), 22 cases ≥10 yr in furniture industry 1.6 (0.4–6.1), 3 cases myeloma or Hodgkin's lymphoma not associated with wood dust exposure or furniture work	other occupational exposures
Teschke *et al*. 1997	54 nasal and 119 bladder cancer cases occurring 1990–1992, frequency matched by age and gender with population controls in British Columbia	personal or phone interviews exposed: pulp and paper, forestry and logging, and sawmill work	OR adj. for age, gender, and smoking: nasal cancer: pulp and paper 3.1 (0.4–25.4), 3 cases forestry 0.5 (0.1–2.4), 2 cases sawmill 0.4 (0.1–1.6), 3 cases bladder cancer: respective nonsignificant ORs 1.5, 1.6, and 1.0 based on 2, 15, and 15 exp. cases	coexposures

Reference	Population	Exposure	Results	Confounders and comments
Cocco *et al*. 1998	1,023 gastric cardial cancer deaths matched by age and region with 5,115 noncancer deaths from 24 U.S. states for 1984–1992	census industry codes from death certificates exposed: 1) pulp and paper, saw and planing mill work 2) ever exposed to wood dust 3) intensity of dust exposure (low, medium, high)	OR adj. for age, marital status, rural residence, and socioeconomic status: by industry for white M: pulp and paper 2.0 (1.0–3.1), 5 deaths sawmill 0.9 (0.3–3.0), 5 deaths by wood dust exposure: ever 0.8 (0.6–1.1), 65 deaths low 0.8 (0.5–1.2), 34 deaths medium 0.9 (0.4–1.8), 9 deaths high 0.9 (0.5–1.4) 22 deaths	diet, smoking,
Cocco *et al.* 1999	41,957 stomach cancer deaths matched by age, race, gender, and region with 83,914 noncancer deaths from 24 U.S. states for 1984–1996	death certificate occupation and industry listings used to estimate intensity of exposure to wood dust (no, low, medium, or high)	OR adj. for age, marital status, rural residence, and socioeconomic status: African-American M: low 1.16 (1.02–1.33), 406 deaths med. 1.10 (0.93–1.32), 206 deaths high 0.80 (0.61–1.04), 80 deaths no other statistically significant associations	diet, smoking
Gustavsson *et al*. 1998	545 cases of squamous-type oral, pharyngeal, laryngeal, and esophageal cancer occurring 1988–1991, frequency matched by age and region with 641 Swedish population controls	interviews used to determine job history and 17 exposures exposed: ever exposed to wood dust	OR adj. for region, age, alcohol, and smoking: all sites 0.62 (0.43–0.90), 69 cases pharyngeal 0.52 (0.27–0.99), 14 cases laryngeal 0.54 (0.32–0.93), 20 cases oral 0.77, esophageal 0.88; not statistically significant	other occupational exposures

Reference	Population	Exposure	Results	Confounders and comments
Andersson *et al*. 1998	all 780 deaths in 3 parishes surrounding sulfite mills in Sweden for 1960–1989; 33 lung, 35 stomach, and 10 brain cancer deaths compared with all other deaths	job titles from death registries exposed: "sulfite worker" or "factory worker"	OR adj. for age: lung 1.4 (0.7–2.6), 10 deaths stomach 0.4 (0.2–0.9), 4 deaths brain 3.3 (1.2–8.9), 5 deaths	smoking, diet, potential coexposures (asbestos, SO_2)
Hoppin *et al*. 1999	231 living, registry-identified, histologically confirmed sarcoma cases diagnosed 1984–1988 in 8 U.S. states, frequency matched by age and registry area with 1,908 randomly selected healthy population controls	telephone interviews for occupational history and specific exposures exposed: 1) sawmill worker 2) plywood worker 3) occupationally exposed to wood dust	OR adj. for ethnicity: wood dust: dermatofibrosarcoma 1.7 (0.8–3.24), 18 exp. cases leiomyosarcoma 2.4 (1.4–4.2), 28 cases liposarcoma 0.6 (0.2–1.2), 9 cases skeletal sarcoma 1.8 (0.9–3.3), 19 cases not adj., for wood dust: malignant fibrohistiocytic sarcoma 0.7 (0.2–1.7), 6 cases sawmill work: all ORs 1.6–2.5, but none statistically significant; ≤ 6 exp. cases plywood work: leiomyosarcoma OR 2.2 (1.3–3.9), 24 cases no risks significantly increased for other cancer types	coexposures

Reference	Population	Exposure	Results	Confounders and comments
Mirabelli *et al*. 2000	43 living persons with histologically confirmed nasal and 92 nasopharyngeal cancer occurring 1984-1988, frequency matched with 2,506 population controls	interviews for occupational exposures to 14 factors exposed: occupationally exposed to wood dust or sawdust	prevalence of exposure: nasal cancer cases 25.6% nasopharyngeal cancer cases 27.2% controls 26.3% chlorophenol (wood preservative) significantly associated with nasopharyngeal cancer, but most exposure occurred among machinists	coexposures, exposure misclassification, smoking
Mao *et al*. 2000	1,469 histologically confirmed non-Hodgkin's lymphomas frequency matched by age and gender with 5,073 cancer-free controls from 8 Canadian provinces, 1994–1997	questionnaires to determine exposure to 17 substances exposed: occupationally exposed to wood dust ≥ 1 yr	OR adj. for age, body mass index, province, and milk consumption: non-Hodgkin's lymphoma: M 0.9 (0.8–1.1), 205 cases F 1.4 (1.0–2.0), 57 cases ORs increased with duration of exposure among women, peaking at 1.7 (1.1–2.6) for ≥ 7 yr	coexposures

Reference	Population	Exposure	Results	Confounders and comments
Vaughan *et al*. 2000	196 incident epithelial nasopharyngeal cancer cases identified from registries in 4 U.S. states during 1987–1993, frequency matched by age, gender, and registry region with 244 population controls selected by random-digit dialing	telephone interviews to establish job histories and specific exposures, including wood dust, and rate cumulative exposure exposed: 1) ever exposed to wood dust 2) cumulative exposure (mg/m^3-years)	OR adj. for age, gender, and race: ever exposed 1.5 (0.7–3.3), 17 cases OR adj. for age, gender, race, formaldehyde exp.: ever exposed 1.2 (0.5–2.7), 17 cases cumulative exposure: 0–2.75 mg/m^3-years 0.7 (0.2–2.5), 5 cases 2.75–15.70 mg/m^3-years 3.0 (0.9–9.8), 10 cases > 15.70 mg/m^3-years 0.4 (0.1–2.3), 2 cases	smoking, drinking, respondent bias adj. for formaldehyde consistently weakened association

4 Studies of Cancer in Experimental Animals

The IARC reviewed evidence for carcinogenicity of wood dusts, alone and in combination with known carcinogens, from studies of inhalation exposure in rats and hamsters, intraperitoneal injection in rats, skin painting in mice, and exposure to wood-shavings bedding in mice (IARC 1995, Appendix A).

4.1 Inhalation exposure in rodents

4.1.1 Rats

No respiratory tract tumors were found in 15 surviving female Sprague-Dawley rats, 11 weeks old at the start of the study, that were exposed by inhalation to untreated beech wood dust (approximately 70% of the particles with a maximal diameter of about 10 μm and 10% to 20% with a diameter of about 5 μm or less) at a concentration of 25 mg/m^3, six hours per day, five days per week, for 104 weeks. Only the nasal cavities of the surviving rats were histologically examined for tumors; no squamous metaplastic or dysplastic lesions were found in the surviving rats. The incidence of tumors outside the respiratory tract, reported for about 50% of the rats, was not different from that in untreated controls (Holmström *et al.* 1989). The IARC Working Group noted the small number of animals and the inadequate reporting of the tumors outside the respiratory tract (IARC 1995).

No wood dust-induced tumors were found in 15 female Wistar rats, four weeks old at the start of the study, exposed by inhalation to beech wood dust (mass median aerodynamic diameter, 7.2 μm; geometric standard deviation, 2.2 μm) at a concentration of 15.3 ± 13.1 mg/m^3, six hours per day, five days per week, for six months, for a total exposure period of 666 hours. The rats were observed for up to 18 months before sacrifice of the survivors. Gross examination of rats and histological examination of their nasal cavities revealed no respiratory tract tumors. Gross examination of the rats and histological examination of their lungs, livers, spleens, and kidneys also showed no difference in the incidence of tumors outside the respiratory tract, compared with the incidence in controls (Tanaka *et al.* 1991). The IARC Working Group noted the small number of animals (IARC 1995).

4.1.2 Hamsters

No respiratory tract tumors were found in 12 male Syrian golden hamsters, 10 weeks old at the start of the study, that were exposed by inhalation to beech wood dust (approximately 70% of the particles with a maximal diameter of about 10 μm and 10% to 20% of the particles with a diameter of about 5 μm or less) at a concentration of 15 mg/m^3, six hours per day, five days per week, for 36 weeks. However, one hamster of the surviving 22 of 24 male Syrian golden hamsters, 10 weeks old, similarly exposed to beech wood dust at 30 mg/m^3 developed an unclassifiable infiltrating nasal tumor, and another animal in this group exhibited cuboidal metaplasia with mild dysplasia of the nasal epithelium. No tumors were reported in the other organs examined (liver and kidney) (Wilhelmsson *et al.* 1985a,b). The IARC Working Group noted the short duration of the study (IARC 1995).

4.2 Intraperitoneal injection in rats

No mesothelioma or sarcoma was found in the abdominal cavities of 52 female Wistar rats exposed to beech wood dust by intraperitoneal injection. The eight-week-old rats were given intraperitoneal injections totaling 250 to 300 mg of beech wood dust (of unspecified particle size) in doses of 50 mg/mL (suspended in 0.9% sodium chloride solution). The surviving rats were sacrificed and examined 140 weeks after the first injection. Other rats similarly administered chrysotile asbestos (which could be considered positive controls for the beech wood dust exposure) developed mesothelioma (Pott *et al.* 1989).

4.3 Skin application of wood dust extracts in mice

A significant dose response in the incidence of skin and mammary gland tumors was seen in female mice exposed to a methanol extract of beech wood dust. Four groups of 70 young female NMRI mice of unspecified age were given skin applications of a mutagenic fraction of a methanol extract of dust from untreated semi-dry beech wood. The extract was dissolved in 30 µl of acetone and applied twice a week for three months to a 1- to 2-cm^2 shaven area of the lower back. Doses were equivalent to 2.5, 5.0, 7.5, or 10 g of wood dust per mouse. Five other groups of mice were used as controls: acetone only, shaven not exposed, unshaven and not exposed, and two groups exposed to benzo[*a*]pyrene (BaP) as positive controls. The survival of the mice exposed to wood dust was not significantly different ($P = 0.571$, Mann-Whitney U test) from that of unexposed controls. Precancerous lesions (epithelial hyperplasia and hyperkeratosis) and benign and malignant tumors of the skin and mammary glands developed in the mice exposed to the wood dust extract or BaP (Mohtashamipur *et al.* 1989). The IARC Working Group noted that a significant dose response for skin tumors was seen in the mice exposed to wood dust, whether or not the analysis included the kerotoacanthoma and papillary cystadenoma. Further, it noted that the incidence of mammary tumors in exposed mice was significantly dose related when mammary gland adenoma, adenoacanthoma, and mixed mammary tumors were combined (IARC 1995). The results of the study are summarized in Table 4-1.

Table 4-1. Tumor incidences in mice dermally exposed to beech wood dust extracts

Tumor	Negative controls			Extract (g)[a]				Benzo[a]pyrene (µg)[b]	
	Untreated (n = 43)	Shaven (n = 44)	Shaven, acetone only (n = 42)	2.5 (n = 43)	5.0 (n = 50)	7.5 (n = 46)	10.0 (n = 49)	5 (n = 43)	10 (n = 42)
Skin									
squamous-cell carcinoma	–	–	–	1	–	–	1[c]	1	15
squamous-cell papilloma	–	–	–	1	1	6	5[c]	2	5
keratoacanthoma	–	–	–	–	–	1	–	–	2
papillary cystadenoma	–	–	–	–	1	–	–	–	–
precancerous skin lesions	–	1	2	2	4	8	6	13	18
Mammary gland									
adenocarcinoma	–	–	–	–	4	3	2[d,e]	1	1
adenoacanthoma	–	–	–	–	–	–	1[d,e]	–	–
mixed tumors	–	–	–	–	–	–	2[d]	–	–

Source: adapted from Mohtashamipur *et al.* 1989; numbers of animals given are effective numbers.
[a]Applied material was a mutagenic fraction of a methanol extract of dust from untreated, semi-dry beech wood.
[b]Positive control.
[c]$P < 0.01$; Cochran-Armitage test for trend, where the incidences of tumors (including both squamous-cell carcinomas and papillomas or papillomas alone) were compared between acetone-only controls and wood dust extract-exposed groups.
[d]$P < 0.02$; Cochran-Armitage test for trend, where the incidences mammary gland adenocarcinoma, adenoacanthoma, and mixed mammary gland tumors were considered.
[e]$P < 0.06$; Cochran-Armitage test for trend, where only mammary adenocarcinoma and adenoacanthoma were considered.

4.4 Exposure of mice via wood-shavings bedding

It was suggested that exposure to cedar wood shavings (used as animal bedding) might play a role in the prominent differences in the incidence of spontaneous mammary and liver tumors in mice (mainly C3H mice) (Schoental and Gibbard 1972, Schoental 1974, both cited in Nylander and Dement 1993; Sabine *et al.* 1973, Sabine 1975, both cited in IARC 1995). The possible carcinogenic effect was attributed to the α, β-unsaturated carbonyl compounds of wood lignins and podophyllotoxin present in the wood shavings (Schoental and Gibbard 1972, Schoental 1974, both cited in Nylander and Dement 1993). However, other studies designed to confirm these observations found no evidence to support the carcinogenicity of wood-shavings bedding (pine sawdust or pine and cedar wood shavings) in this strain of mice. Instead, it was suggested that differences in the conditions of animal maintenance (including food consumption, infestation by ectoparasites, and general condition of health) were responsible for the differences in the incidence of these spontaneous tumors in the C3H, SWJ/Jac, and HeJ mouse strains (DePass *et al.* 1986, cited in Nylander and Dement 1993; Heston 1975, Vlahakis 1977, Jacobs and Dieter 1978). No control groups were used in these studies.

4.5 Coadministration with known carcinogens in rodents

In the inhalation exposure study by Holmström *et al.* (1989) described in Section 4.1.1, female Sprague-Dawley rats were similarly exposed to a combination of untreated beech wood at a concentration of 25 mg/m^3 and formaldehyde at a concentration of 15.2 ± 1.2 mg/m^3. Of 15 exposed rats, 8 exhibited pronounced squamous hyperplasia, with or without keratinization of the nasal epithelium at the level of the nasoturbinates and maxillary turbinates; the pronounced squamous hyperplasia in 4/15 of these rats were accompanied by dysplasia of the nasal epithelium. Pronounced squamous hyperplasia, with or without keratinization of the nasal epithelium at the level of the nasoturbinates and maxillary turbinates, also was found in 9/16 rats exposed to formaldehyde at 14.9 ± 1.3 mg/m^3; the pronounced squamous hyperplasia in 1/16 of these rats was accompanied by dysplasia of the nasal epithelium. The incidence of tumors outside the respiratory tract, reported for about 50% of the rats, was not different from that of untreated controls. The IARC Working Group noted the small number of animals and the inadequate reporting of the tumors outside the respiratory tract (IARC 1995).

In the inhalation exposure study by Tanaka *et al.* (1991) described in Section 4.1.1, five rats exposed to wood dust were then immediately exposed to sidestream cigarette smoke (from 10 cigarettes per day) at a concentration of 10.2 mg/m^3, two hours per day, five days per week, for one month, and observed for up to 18 months. Gross examination of rats and histological examination of their nasal cavities revealed no respiratory tract tumors, and the incidence of tumors outside the respiratory tract did not differ from that in controls. The IARC Working Group noted the small number of animals in the study and the relatively short treatment and observation periods (IARC 1995).

4.5.1 Hamsters

In the inhalation exposure study by Wilhelmsson *et al.* (1985a,b) described in Section 4.1.2, two additional groups of hamsters were similarly exposed to wood dust at a concentration of 15 mg/m^3 for 36 weeks and also received weekly subcutaneous

injections of 1.5 mg of *N*-nitrosodiethylamine (NDEA) for 12 consecutive weeks. Tracheal squamous-cell papillomas occurred in 4/8 hamsters treated with the combination of wood dust and NDEA, 3/8 hamsters treated with NDEA alone, and 1/7 control hamsters. Hamsters similarly exposed to wood dust at 30 mg/m^3 and given weekly subcutaneous injections of 3.0 mg of NDEA for 12 consecutive weeks developed respiratory tract tumors at an incidence not significantly different from that in hamsters exposed only to NDEA. Mortality was high in all groups and significantly higher in NDEA-exposed animals ($P < 0.05$, Fisher's exact test). The IARC Working Group noted the short duration of the study, the small number of animals in each group, the absence of data on mortality rates, and the high losses of animals and tissues due to cannibalism (IARC 1995).

4.6 Summary

No respiratory tract tumors were found in female Sprague-Dawley rats, female Wistar rats, or male Syrian golden hamsters exposed to wood dust via inhalation. No mesotheliomas or sarcomas were detected in the abdominal cavities of rats given intraperitoneal injections of wood dust. Wood shavings used as animal bedding did not significantly contribute to the incidences of spontaneous mammary and liver tumors in mice (strains C3H, SWJ/Jac, and HeJ). Similarly, inhalation exposure to wood dust did not significantly affect the incidence of respiratory tract tumors induced by formaldehyde in female Sprague-Dawley rats, sidestream cigarette smoke in female Wistar rats, or NDEA in male Syrian golden hamsters. However, a significant dose-response relationship was found for skin tumors (squamous cell carcinoma and papilloma) and mammary tumors (adenocarcinoma, adenoacanthoma, and mixed tumors) in female NMRI mice dermally exposed to a methanol extract of wood dust.

5 Genotoxicity

The IARC reviewed the literature through 1994 regarding the genotoxicity of wood dust (IARC 1995), the results of which are summarized in Table 5-1. Only a few studies using test systems other than the Ames assay were available for review by the IARC. Relevant genotoxicity studies published after the IARC (1995) monograph are discussed in Sections 5.3 and 5.4 and summarized in Table 5-2. The IARC monograph is included in Appendix A.

Table 5-1. Genetic and related effects of wood dust or wood fume exposure as reviewed in IARC (1995)

Test system	End point	Results	References
Prokaryotic			
Salmonella typhimurium	reverse mutation (strains TA98, TA100)	variable negative to weak positive (extracts of various wood dusts, with and without metabolic activation)[a]	Brockmeier and Norpoth 1981, McGregor 1982, Mohtashamipur *et al*. 1984, 1986, Kubel *et al*. 1988, Weissmann *et al*. 1989, Mohtashamipur and Norpoth 1990
Salmonella typhimurium	reverse mutation (strains TA98, TA100, TA102)	negative (birch and spruce dusts, with and without metabolic activation)	Kurttio *et al*. 1990
Mammalian *in vitro*			
Rat hepatocytes	DNA damage	weak positive (beech dust, without metabolic activation)	Schmezer *et al*. 1994
		positive (oak dust, without metabolic activation	
		positive (particle board dust, without metabolic activation)	
		negative (spruce dust, with or without metabolic activation)	
Mammalian *in vivo*			
Mice	micronuclei (duodenal crypts)	positive (beech dust)	Mohtashamipur and Norpoth 1989
Rats	micronuclei (nasal epithelial cells)	positive (beech dust)	Nelson *et al*. 1993
Humans	chromosomal aberrations (peripheral lymphocytes)	positive (heated wood fumes[b])	Kurttio *et al*. 1993

Source: adapted from IARC 1995

[a]Weak positive results were reported for dust of ash, beech, oak, and limba, obeche, and walnut. Tests with birch, chestnut, elm, mahogany, and spruce dust all gave negative results.

[b]Nonsmoking plywood factory workers exposed to fumes emitted from heated wood. Wood dust exposure was not mentioned.

5.1 Prokaryotic systems

No additional information on the genotoxicity of wood dust in prokaryotic systems was found in the published literature. The IARC (1995) also reviewed Ames assay results for several compounds that occur naturally in wood. These included Δ^3-carene, coniferyl alcohol, deoxypodophyllotoxin, 2,6-dimethoxybenzoquinone, eugenol, quercetin, scopoletin, 3,4,5-trimethoxycinnamic acid, and vanillic acid. Δ^3-Carene gave weak positive results in *Salmonella typhimurium* strains TA100 and TA98 and negative results in strain TA102. Results were negative in all three strains when an exogenous metabolic activation system was used. Quercetin gave positive results (with exogenous metabolic activation) for strains TA100, TA1538, and TA98. All other test results were negative.

5.2 Plants and lower eukaryotic systems

No information on the genotoxicity of wood dust in plant systems or lower eukaryotic systems was found in the published literature.

5.3 Mammalian systems

5.3.1 In vitro *assays*

5.3.1.1 Chromosomal aberrations in human embryonic lung cells

Solvent extracts of untreated wood dust (beech, oak, and pine) were evaluated for their ability to induce chromosomal aberrations in human MRC-5 embryonic lung cells (Zhou *et al.* 1995). Cells were exposed to three or four concentrations per extract, with or without S9 metabolic activation. No dose-dependent activity was observed with any extract in the presence of S9; however, in the absence of S9, dose-dependent chromosome breaks (oak extracts) and chromatid breaks (beech and oak extracts) were observed. The researchers concluded that hardwood dust might contain some genotoxic and possibly carcinogenic components.

5.3.2 In vivo *assays*

5.3.2.1 Micronucleus induction in human peripheral blood lymphocytes

Peripheral blood lymphocytes in workers exposed to the dust of poplar and linden wood were examined for micronuclei (Jiang *et al.* 1994). The study group consisted of 298 workers (163 male and 135 female) employed at match factories. Workers were grouped by years of employment (0 to 5 years, 5 to 10 years, and > 10 years). The control group included 45 restaurant waiters (24 male and 21 female). The average frequency of induced micronuclei was 36.2% in the exposed group (range 13.5% to 54.6%), compared with 4.4% in controls. There was no relationship between the quantity of smoking and micronucleus frequencies. These researchers speculated that the volatile and unstable substances in the wood dust were responsible for the observed effects.

5.3.2.2 DNA damage and repair in human lymphocytes and leukocytes

Palus *et al.* (1998) reported DNA damage in peripheral blood lymphocytes of 24 workers (13 male and 11 female) in a wooden furniture plant in southeastern Poland. The length of employment ranged from 1 to 30 years, with an average of 15.9 years. The control group consisted of 13 office workers at the furniture plant and 15 employees from a medical facility. DNA single-strand breaks were determined by the microfiltration

method, and DNA repair was determined by ^{3}H incorporation into DNA. A statistically significant increase in DNA single-strand breaks and DNA repair was observed in workers exposed to wood dust and other substances emitted by furniture coating materials. The mean percentage of DNA damage in the exposed workers was 24.1% (7.3% to 48.4%), compared with a mean of 13.3% in controls. Single-strand breaks were significantly more frequent in workers who smoked than in controls who smoked or in nonsmoking workers. Nonsmoking workers had a slightly but not significantly higher frequency of single-strand breaks than did nonsmoking controls. Smoking did not increase the frequency of single-strand breaks in the controls. These data suggested that exposure to wood dust (and/or to substances emitted by furniture coating materials) could cause DNA damage, and that smoking could intensify the effect.

In a subsequent study at the same furniture plant, Palus *et al.* (1999) reported a higher incidence of DNA damage in the white blood cells of 35 workers (14 male and 21 female). The length of employment ranged from 1.4 to 30 years, with an average of 16.6 years. Controls were 20 furniture plant office workers and 21 employees from a medical facility. The comet assay (single-cell gel electrophoresis) was adapted to detect DNA damage. The mean percentage of DNA damage in the exposed group was 21.5% (11% to 39%), compared with 9.7% in controls. DNA damage was similar among smoking (22.1%) and nonsmoking workers (20.8%), but was significantly higher in the smoking controls (13.2%) than the nonsmoking controls (7.0%). In a parallel experiment, the comet assay was used to measure the DNA repair efficiency of the exposed leukocytes. After a one-hour incubation in RPMI 1640 medium, 20% of the damaged DNA was repaired in the exposed group, compared with 25% in the control group, a statistically significant decrease in DNA repair efficiency. Wood dust exposure was identified as a possible etiologic agent.

5.4 Other tests (*in vivo* and *in vitro*)

Archived sinonasal carcinoma tissue from 28 male patients was examined for point mutations at codons 12, 13, and 61 of the K-*ras* protooncogene (Saber *et al.* 1998). Of these patients, 16 had been occupationally exposed to wood dust; one patient had been a wood carver, one had manufactured parquetry, and the rest had manufactured wooden furniture. Most of them had practiced their trade for several decades. The remaining patients did not have a history of wood dust exposure. Four K-*ras* mutations were detected in the 28 tumor tissue samples. The two mutations detected in tumors from patients exposed to wood dust both were G:C to A:T transitions at codon 12. One of these patients had worked as a furniture maker for 10 years and as a carpenter for 30 years. The other had worked as a furniture maker all his life. The researchers concluded that the relatively high proportion of this type of mutation could indicate the presence of a genotoxic agent.

In a similar study, mutations at codons 12, 13, and 61 of the K-*ras*, H-*ras,* and N-*ras* protooncogenes were studied in 31 male patients diagnosed with ethmoid sinus adenocarcinoma (Pérez *et al.* 1999). Of these patients, 25 had histories of occupational wood dust exposure, ranging from 3 to 50 years (average 32 years). Identical H-*ras* mutations in codon 12 (all T to G transversions) were found in five cases but showed no association with the patients' previous exposure to wood dust. A single K-*ras* mutation

(GGT to GAT at codon 12) and no N-*ras* mutations were observed. The H-*ras* mutation was associated with a subgroup of patients with ethmoid sinus adenocarcinoma for whom the prognosis was poor.

Table 5-2. Recent studies of genetic and related effects of wood dust exposure

Test system	End point	Results	References
Mammalian *in vitro*			
Human MRC-5 embryonic lung cells	chromosomal aberrations	positive (oak and beech dust without S9)	Zhou *et al.* 1995
		negative (pine dust with and without S9, beech and oak dust with S9)	
Mammalian *in vivo*			
Humans	micronuclei in peripheral blood lymphocytes	positive (poplar and linden dust)	Jiang *et al.* 1994
Humans	DNA damage in peripheral blood lymphocytes and white blood cells	positive	Palus *et al.* 1998, 1999
Other tests			
Humans	K-*ras* mutation in nasal tumors	positive[a]	Saber *et al.* 1998
Humans	K-*ras* and H-*ras* mutations in nasal tumors	positive[b]	Pérez *et al.* 1999

[a]Four mutations detected in 28 tumors. Two of the mutations were in patients with a history of wood dust exposure.
[b]Five H-*ras* mutations and one K-*ras* mutation detected in 31 tumors. Mutations were not associated with exposure to wood dust.

5.5 Summary

The Ames assay was used to test extracts of various wood dusts for mutagenicity. Weak positive results for reverse mutation in *Salmonella typhimurium* were reported for dusts of a few hardwoods, particularly beech. In addition, two chemicals found in wood, Δ^3-carene and quercetin, were mutagenic in the Ames assay.

In vitro and *in vivo* tests in mammalian systems gave positive results for DNA damage (primarily single-strand breaks and repair), micronucleus induction, and chromosomal aberrations (primarily chromatid breaks).

6 Other Relevant Data

An association of wood dust exposure and nasal cancer was first reported in England in the mid 1960s. Subsequent studies in other countries supported this finding. In general, the data suggest that the excess risk of nasal cancer is associated with chronic, high-level exposures. To date, the specific causative agents, risk factors, and mechanism of cancer induction are not well understood (Nylander and Dement 1993). The available data on the deposition, clearance, and retention of wood dust and possible mechanisms are reviewed in this section.

6.1 Deposition, clearance, and retention

No specific studies on the deposition, clearance, and retention of wood dust in humans or animals were reviewed by the IARC (1995) or found in the published literature. However, data from other particle deposition studies are useful. Most particles larger than 10 µm are deposited in the nasopharyngeal region and are removed by mucociliary transport. Smaller particles are deposited in the tracheobronchial or alveolar regions of the lungs, depending on the particle size, flow rates, type of breathing (nose, mouth, or a combination), and inter-individual variation (IARC 1995, Demers *et al.* 1997).

The sizes of wood dust particles vary depending on the type of wood and particular woodworking operation (e.g., sawing or sanding). In general, most woodworking operations produce mainly particles > 10 µm and relatively low concentrations of respirable dust (< 5 µm); therefore, substantial amounts are deposited in the nasal cavity (Nylander and Dement 1993).

Wood dust particles are deposited primarily in two areas in the nasal cavity: (1) a small, oval-shaped area at the lower anterior part of the nasal septum near the floor of the nose and (2) the lower anterior end of the middle turbinate (Nylander and Dement 1993). Several studies have shown lower mucociliary transport (clearance) rates in workers exposed to wood dust than in a control group. Decreased clearance rates from the nasopharyngeal region in workers were concentration dependent, and in some cases, clearance took at least two days after exposure had ceased (IARC 1995).

6.2 Possible mechanisms

No specific chemical or physical properties of wood dust (or combination of properties, either of wood dust alone or of wood dust and other agents) have been associated with the development of nasal cancer in humans. The two primary hypothetical links between wood dust exposure and nasal cancer are (1) inhalation of carcinogenic chemicals present in the wood (such as tannins, aldehydes, and other chemicals naturally present in the wood or added during processing) and (2) inhalation of wood dust particles themselves (Nylander and Dement 1993). The strongest association between wood dust exposure and nasal cancer comes from chronic occupational exposure to hardwood dust without chemical additives (Nylander and Dement 1993, Demers *et al.* 1997). Furniture making and cabinet making, factory joinery, and carpentry are the occupations associated with the greatest risk of nasal adenocarcinoma of the ethmoidal sinuses, an otherwise rare tumor type. Although adenocarcinoma is most frequently associated with wood dust

exposure, squamous-cell carcinoma of the maxillary sinus is more common in Japanese woodworkers (for reasons unknown) and has been associated with chronic exposure to softwood dust (Nylander and Dement 1993).

6.2.1 Chemicals in wood

Chemical substances in wood can include both natural substances (e.g., tannins or aldehydes) or exogenous substances added during wood processing (e.g., chlorophenols). Tatrai *et al.* (1995) identified cellulose in pine wood dust as the agent possibly responsible for pulmonary inflammation and fibrosis. Bianco and Savolainen (1994) demonstrated that tannin concentrations were higher in hardwoods than softwoods. Tannin extracts were carcinogenic in laboratory animals (Kirby 1960, cited in Bianco and Savolainen 1994).

In some studies with mice, the possible carcinogenic effect of wood was attributed to the α, β-unsaturated carbonyl compounds of wood lignins and podophyllotoxin present in wood shavings (Schoental and Gibbard 1972, Schoental 1974, both cited in Nylander and Dement 1993). However, subsequent findings in mouse studies have not supported this conclusion (DePass *et al.* 1986, cited in Nylander and Dement 1993; Heston 1975, Vlahakis 1977, Jacobs and Dieter 1978, all cited in IARC 1995).

Although no specific chemical or physical agents have been directly associated with nasal cancer in woodworkers, wood dust exposure has been associated with inflammatory reactions and other effects within the nose and lungs (Nylander and Dement 1993, Tatrai *et al.* 1995, Åhman *et al.* 1996, Dahlqvist *et al.* 1996, Wintermeyer *et al.* 1997). Chronic exposure to particulate matter can cause irritation and inflammation that initiates an apoptotic process and leads to accelerated cell death and cell replacement. In response, increased mitogenesis to replace the lost cells increases the probability of clonal expansion of spontaneous mutations, leading to tumor development (Nylander and Dement 1993).

6.2.2 Mucostasis, metaplasia, and dysplasia

Mucostasis could conceivably enhance the carcinogenic effect of wood dust by increasing the residence time of dust particles in the nose. The increased residence time would allow more time for penetration or absorption of chemicals in the wood into the nasal mucosa. In addition to reduced mucociliary clearance, chronic exposure to wood dust has been associated with metaplasia and dysplasia of the nasal epithelium. Biopsies from furniture workers have shown both squamous and cuboidal dysplasia of the nasal epithelium. Although squamous-cell dysplasia may lead to squamous-cell carcinoma, and cuboidal dysplasia may lead to adenocarcinoma, a direct link has not been established (Nylander and Dement 1993, Kuper *et al.* 1997, Blot *et al.* 1997). Indirect evidence includes a Swedish study that reported cuboidal metaplasia and dysplasia adjacent to nasal adenocarcinomas in the majority of 22 wood dust exposed patients (Blot *et al.* 1997).

6.3 Summary

Although it has been hypothesized that the carcinogenic effect of wood dust is due to tannins, aldehydes, or other chemicals present in the wood or added to the wood during processing, the role of the chemical composition of the wood (natural or added) in carcinogenesis induced by wood dust is unclear. The particulate nature of wood dust also may contribute to associated carcinogenesis, because dust generated by woodworking typically consists of a high proportion of particles that are deposited in specific areas in the human nasal cavity. Chronic exposure to wood dust particulates may result in decreased mucociliary clearance and enhance inflammatory reactions in the nasal cavity.

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Appendix B: IARC (1987) Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. Suppl. 7. PP 378 –387.