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Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14, P.O. Box 12233
Research Triangle Park, NC 27709

Re: Call for Public Comments on 8 Nominations, Proposed for Listing or Delisting from the Report on Carcinogens, Tenth Edition, 66 Fed. Reg. 13334 (March 5, 2001)

Dear Dr. Jameson:

The following comments are submitted on behalf of the members of the Inter-Industry Wood Dust Coordinating Committee (IWDCC), in response to the National Toxicology Program (NTP) request for comments on eight nominations proposed for possible listing or delisting in the Report on Carcinogens (RoC), Tenth Edition. The IWDCC compromises more than twenty trade associations having an interest in wood dust health issues.

These comments are the latest IWDCC submission directed to the proposed listing of wood dust in the Tenth RoC. For the reasons detailed in our previous comments of June 5, 2000 (copy attached) and briefly restated below, we submit that the evidence does not support the listing of wood dust in the RoC as a known carcinogenic risk to workers or the general population in the United States. While older European studies have shown sizable excesses of nasal cancer in workplaces where wood dust and other confounding exposures were present, the weight of the cohort and case control studies in North America does not suggest an excess risk of nasal cancer. Neither six cohort studies collectively examining over 85,000 workers, nor the weight of over a dozen case control studies, show an excess risk in North America.

We therefore urge NTP to abandon the proposed classification, since the RoC is intended to evaluate hazards in the United States. Should NTP nonetheless proceed with the proposed listing, it is important NTP clearly distinguish evidence from the European studies from the North American studies in order to clearly articulate the weight of the evidence in the United States. We therefore request the inclusion of language within the RoC characterizing the epidemiological data underlying the listing.

The attached IWDCC comments included a submission from William Blot, Ph.D., who evaluated the epidemiological studies NTP reviewed when considering the listing of wood dust as a known human carcinogen. In his comments, Dr. Blot highlighted several reasons why the literature does not support a conclusion of risk in the North America.

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A number of European studies reported substantial excess levels of nasal cancer primarily among workers exposed to hardwood dust. Although only a few of these studies included quantitative exposure data, the available information indicates that the elevated risk of nasal cancer occurred at high levels of exposure not found today in the United States. Furthermore, some of the European studies provide evidence that several compounds other than wood dust may have contributed to the increased risk.

In 1997, Dr. Blot and his colleagues published an article in the *Journal of Occupational and Environmental Medicine* (JOEM, citation in attachment), comparing the epidemiological evidence on nasal cancer among woodworkers in North America and Europe. While we need not repeat that review in detail, a brief summary of the relevant conclusions is appropriate.

Blot et al. noted that cohort studies of North American woodworkers found the number of nasal cancers approximately equal to that expected. As the attached Table 1 from the Blot et al. study shows, out of 85,867 workers exposed in these studies, 5 cases of nasal cancers were observed versus 5.2 expected. Only one of the six cohort studies showed an excess (2 cases observed versus one expected.)

The North American case control studies showed mixed results with some showing a negative association and others showing only a minimally positive association. Those with positive associations did not approach the level of excess observed in European woodworkers.

Moreover, studies of North American woodworkers published since the Blot et al. article further support the conclusion that wood dust exposure in the North America does not present the carcinogenic risk reported in Europe. We have updated the attached tables to include publications subsequent to the 1997 *JOEM* publication, which were summarized in Dr. Blot's December 2000 remarks to the NTP Board of Scientific Counselors. The two most recent case-control studies, Teschke (1997) and Mirabelli (2000), do not show elevated risks. Of the five studies published in the 1990's, only Vaughn (1991) showed an excess, and that was not statistically significant. Looking at all 12 case-control studies, it is noteworthy that the elevated relative risk of nasal cancer based on eight cases of furniture workers in a 1977 Brinton et al. study was not replicated in a subsequent 1984 Brinton et al. study. The 1977 study relied only on death certificates, while the 1984 study by the same authors of workers in the same geographic region incorporated interview information and found a nasal cancer deficit among furniture workers. Although the authors did report an elevation of nasal adenocarcinoma, there was also a deficit of squamous cell carcinoma. Therefore, one must interpret the histological data cautiously.

Clearly, when viewed in totality, the weight of the evidence does not indicate a cancer hazard to U.S. workers. The NTP Report is designed to address and to communicate with the U.S. population. For these reasons, we renew our objections to the NTP proposal to list wood dust as a known human carcinogen. The studies indicate substantial differences in conditions affecting the European versus North American populations. We urge the NTP to reconsider the proposed classification after thoroughly examining the literature on North American occupational exposures.

Should NTP nonetheless proceed with the proposed classification, we encourage NTP to include within the RoC entry an accurate characterization of the findings upon which the classification rests. The Tenth RoC should accurately characterize the epidemiological findings to reflect that:

- The data supporting classification of wood dust as a carcinogen derive primarily from European studies, and given differing workplace conditions and study results, may not be relevant to the U.S.; the weight of the evidence from studies in North America does not support such a classification.
- Many of the European studies that showed substantial excess risk were based on data initially collected in the 1960's from exposures occurring before World War II, and, therefore, may have limited relevance to current workplace exposure scenarios.
- Observed excesses tended to be in workplaces where workers may have been exposed to several confounding exposures.
- The weight of multiple cohort studies of over 85,000 workers, and a dozen case control studies, does not suggest an excess risk of nasal cancer in North America.

The purpose of the proposed NTP listing is to characterize the possible carcinogenic hazard associated with exposure to wood dust in the United States. Given the disparity between the European and North American epidemiological evidence, it is imperative that the RoC accurately reflect the state of the evidence and its relevance to the intended U.S. audience of the RoC. To do otherwise could result in adverse social and economic consequences without any attendant gain in occupational or environmental health.

We appreciate your consideration.

Sincerely,

John L. Festa

John L. Festa, Ph.D.
Senior Scientist

Enclosures

Table 1. Nasal cancer in North American cohort studies of wood-dust exposed workers
(Blot et al. (1997), Table 1, as updated by Dr. Blot for Dec. 2000 Board of Scientific Counselors meeting)

First Author (year)	Industry	No. of Workers	No. of Nasal Cancers	
			Observed	Expected
Stellman (1984)	Wood Workers	10,322	2	1.0
Miller (1989, 1994)	Furniture	34,801	2	2.5
Blair (1986)	Plywood	2,309	0	Unknown
Robinson (1990)	Plywood	2,283	0	0.4
Roscoe (1992)	Model makers	2,294	0	0.3
Stellman (1998)	Wood dust exposed	33,858	1	1.0
TOTAL			**5**	**5.2**

Table 2. North American case-control interview studies of nasal cancer in relation to wood dust exposure (from Blot et al. (1997), updated through 2000)

First Author (year)	Industry	No. of exposed cases	RR	95% CI
Ball (1967)	Wood workers	28	1.2	0.6-2.2
Brinton (1977)	Furniture	8	4.4	1.3-15
	Other	5	1.5	0.4-4.3
Roush (1980)	Wood-related	8	4.0	1.5-11
Elwood (1981)	Wood-related	28	2.5	1.0-4.5
Finkelstein (1989)	Wood-related	9	1.9	0.7-5.4
Viren (1989)	Wood-related	30	1.5	0.9-2.5
	Lumber	22	2.0	1.0-3.4
	Furniture	7	1.0	0.4-2.8
Studies Obtaining Occupational Histories and Risk-Factor Data from Questionnaires				
Brinton (1984)	Furniture	8	0.8	0.3-2.0
	Lumber	26	1.4	0.7-2.6
	Carpentry	13	1.5	0.6-3.4
	Other Wood	3.0	0.6	0.1-2.3
Vaughan (1991)	Wood-related	7	2.4	0.8-6.7
Mack (1995)	Wood-related	1	0.2	0.0-1.5
Zheng (1993)	Wood-related	8	1.7	0.6-4.3
Teschke (1997)	Wood dust exposed	6+	0.7	0.3-1.6
Mirabelli (2000)	Wood dust exposed	11	1.0	0.5-2.0

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June 5, 2000

VIA FACSIMILE (919-541-0144) and U.S. MAIL DELIVERY

Dr. C. W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14, P.O. Box 12233
Research Triangle Park, NC 27709

Re: Call for Public Comments on Substances, Mixtures and Exposure Circumstances Proposed for Listing in the Report on Carcinogens, Tenth Edition, 65 Fed. Reg. 17889 (April 5, 2000)

Dear Dr. Jameson:

The following comments are submitted on behalf of the members of the Inter-industry Wood Dust Coordinating Committee (IWDCC), in response to the National Toxicology Program's (NTP) announcement of its intent to review additional agents, substances, mixtures and exposure circumstances for possible listing in the Report on Carcinogens (RoC), Tenth Edition. The IWDCC comprises more than twenty trade associations having an interest in wood dust health issues. Member associations represent the full spectrum of the wood and wood products industry. The IWDCC's comments are directed to the proposed listing of wood dust in the Tenth RoC. For the reasons discussed below and in the attached Comments of Dr. William J. Blot, we submit that the evidence does not support listing of wood dust in the RoC.

It appears from the Federal Register notice that the nomination, put forward by the Occupational Safety and Health Administration (OSHA), is based on the 1995 designation of

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wood dust as carcinogenic to humans by the International Agency for Research on Cancer (IARC). 65 Fed. Reg. at 17891. As noted in the attached comments of Dr. William J. Blot (Blot Comments), the IARC classification rested on studies that showed excesses of nasal adenocarcinoma, a rare form of cancer, among woodworkers and furniture makers. Two years after the IARC report, Dr. Blot reviewed the epidemiologic evidence on nasal cancer among wood dust-exposed populations in the U.S. and Europe. The review, which was published in the Journal of Occupational and Environmental Medicine (JOEM, citation provided in attachment), examined the studies relied upon by IARC as well as more recent work reported in the literature. Blot et al. found a striking difference between the European and U.S. studies. Unlike the marked excess of nasal adenocarcinoma observed in woodworkers in the European studies, cohort studies of U.S. wood dust-exposed groups do not show excesses of nasal cancer. Further, as pointed out in the attached Comments, wood dust associations from U.S. and Canadian case-control studies of nasal cancer tend not to be strong and are not consistent across studies.

Closer scrutiny of the European studies indicates that the reported excess nasal cancer risk is associated with significantly higher exposure levels, dating primarily from older (pre-1950) European occupational settings, than are representative of the U.S. workplace today. In addition, there is evidence that the presence of compounds besides wood dust may have contributed to the findings.

An examination of work published since the time of the Blot et al. JOEM review raises further questions about the appropriateness of applying IARC's classification to the U.S. workplace. Referencing the one additional American study that has been published since 1997, a study of 45,000 men with wood dust employment or exposure, Dr. Blot notes that, like the

previous U.S. studies, no excess of nasal cancer was observed (Stellman et al., citation in attachment). In fact, the divergence is so striking between the European studies and the body of U.S. literature, that after reviewing the different findings Dr. Blot observed, "if the IARC in 1995, or today, had to evaluate the potential carcinogenicity of wood dust based only on North American data, in my judgment it would not have classified wood dust as a Group 1 human carcinogen."

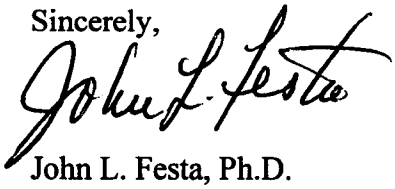
Nor does there appear to be a credible indication of increased rates of other types of cancer among wood dust-exposed groups. The 1995 IARC monograph found little consistent evidence of such excesses. In a 1998 technical report (citation in attachment), IARC investigators noted an increased number (9 observed compared to 3.8 expected) of nasopharyngeal cancers (NPC), and hypothesized that this increase would be plausible because of the proximity of the nasopharynx to the nasal cavity and sinuses. However, as Dr. Blot has observed, this hypothesis is contradicted by the fact that NPCs are almost entirely squamous cell and transitional cell cancers rather than adenocarcinomas. In view of the findings in the IARC survey that the observed nasal cancer association was specific for adenocarcinoma and that woodworkers had no excess at all of squamous cell cancer, there is no logical bridge to an expectation that wood dust would cause nasopharyngeal squamous cell carcinoma. Interestingly, the report found a substantial deficit of non-NPC pharyngeal cancers, which resulted in an overall observation of 17% fewer pharyngeal cancers than expected. Dr. Blot suggests that in light of the deficit for this region, the excess of NPC may be a statistical aberration, perhaps resulting from the multiple comparisons and subdivisions made in the technical report.

Dr. Blot's analysis also notes the absence of excess NPC risk reported in a new study of U.S. woodworkers that was published last month (Vaughan et al., citation in attachment). This multi-center case-control study found no excess risk among those occupationally exposed to wood dust, and further, no trends of rising risk with increasing exposure.

The IARC monograph did not find a causal relationship between wood dust and lung cancer. The 1998 Stellman et al. paper reported 14-17% higher rates of lung cancer among wood dust-exposed workers, but the authors attributed this small excess in part to concurrent asbestos exposure and concluded that "no other convincing associations between wood dust exposure or employment in woodworking occupations and the risk of common cancers were observed."

We urge the NTP reviewers to conduct a thorough examination of the literature, particularly considering the U.S. studies, which are more reflective of occupational exposure in this country today than are the predominantly higher-exposure European studies on which the IARC review relied. We submit that a full and fair review will make it clear that the evidence does not indicate that wood dust poses a carcinogenic hazard to North American workers and thus should not be listed by NTP.

Sincerely,



John L. Festa, Ph.D.
Senior Scientist

Enclosure

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COMMENTS OF WILLIAM J. BLOT, Ph.D.

on behalf of
AMERICAN FOREST & PAPER ASSOCIATION

May 31, 2000

COMMENTS OF WILLIAM J. BLOT, Ph.D.
Prepared on Behalf of the American Forest & Paper Association

The following comments review the epidemiologic literature on rates of cancer among persons exposed to wood dust in the context of the proposed listing of wood dust in National Toxicology Program (NTP) Report 10. I understand that wood dust has been nominated on the basis of the International Agency for Research on Cancer (IARC) classification of wood dust as a recognized human carcinogen in 1995[1]. The IARC designation was based on studies that observed elevated risks of nasal adenocarcinoma, a very rare form of cancer, among woodworkers, mostly hardwood furniture and cabinet makers, in Europe. The NTP likewise cites the reported nasal cancer excess as the reason for the proposed Report 10 listing.

In 1997 my colleagues and I published an article in the Journal of Occupational and Environmental Medicine (JOEM) reviewing the epidemiologic evidence on nasal cancer among wood dust exposed populations[2]. This review surveyed the European and U.S. literature, including the studies relied upon by IARC as well as more recent work. My colleagues and I found that in contrast to the marked excess of nasal adenocarcinoma among groups of woodworkers observed in Europe, cohort studies of American wood dust exposed groups do not reveal excesses of nasal cancer, and wood dust associations from US and Canadian case-control studies of nasal cancer tend not to be strong and differ across studies. Further, although quantitative wood dust exposure data are generally unavailable, general dose information in European studies suggests that the excess risk of nasal cancer is associated with high levels of exposure. There is also evidence that several compounds besides wood dust may have been involved in the clustering of excess cancer in the European studies.

In our JOEM review[2] , we described the strong evidence of increased risk of nasal cancer among European woodworkers, dating initially from the late 1960s from the furniture making center of High Wycombe, England. Ordinarily, this cancer is very rare, with adenocarcinomas of the nasal cavities and sinuses even rarer since the predominant nasal cell type is squamous cell carcinoma. Reports in the 1970s-1990s from the Netherlands, Italy and elsewhere in Europe confirmed the association of elevated risk of nasal cancer among wood dust exposed workers. In each case, the association was specific for adenocarcinoma. In meta-analytic reviews of the totality of available evidence by the 1990s, it was confirmed that woodworkers had no excess at all of squamous cell cancer, but a greater than 10-fold increase in nasal adenocarcinoma[3,4].

In sharp contrast, we noted that no concomitant excess has been seen in North America. Indeed, among several cohort studies tracking cancer among wood dust exposed groups, the number of nasal cancers observed has been approximately equal that expected based on general population rates. In case-control studies examining the issue, results have been mixed and inconsistent (some negative and some mildly positive), and none of the few positive studies indicated excesses anywhere near what had been observed in Europe. We noted that, although most studies did not have quantitative data on levels of wood dust exposure, the European studies that did tended to show excess risks only at the highest doses (which primarily occurred prior to 1950).

Information arising in the few years since our JOEM report has not changed the conclusion that the situation in the United States is far different from that which existed in Europe and was reflected in the studies on which IARC relied. One additional American cohort study has been published, and it too showed no excess of nasal cancer among 45,000 men with wood dust employment or exposure [5]. If the IARC in 1995, or today, had to evaluate the potential carcinogenicity of wood dust based only on North American data, in my judgment it would not have classified wood dust as a Group 1 human carcinogen.

The intent of a proposed NTP listing of wood dust in Report 10 is presumably to warn of a possible hazard of wood dust exposure. Because of the wide disparity between American and European epidemiologic findings, such a warning is not as simple and uncomplicated as it might appear. Indeed, the warning is not needed for Americans since a nasal cancer hazard has not been demonstrated for wood dust exposures in the United States. Issuing a warning when one, based on the American experience, may not be needed seems unlikely to be a beneficial course of action and could have adverse economic or social effects without any net gain in public safety or health.

The IARC review noted that there was little consistent evidence for increased rates of other types of cancer among wood dust exposed groups [1]. In a technical report subsequent to the 1995 monograph on wood dust, IARC investigators noted an increased number of nasopharyngeal cancers (NPC) among wood working cohorts [6]. In combination, there were 9 observed NPC cases vs 3.8 expected, and it was speculated that an increase in these cancers would be plausible because of the anatomic proximity of the nasopharynx and nasal cavity and sinuses. This hypothesis is not credible, however, since NPCs are almost entirely squamous cell and transitional cell cancers, not adenocarcinomas. If wood dust does not cause squamous cell carcinomas in the sinonasal passage, it would not be expected that wood dust exposure would result in nasopharyngeal squamous cell carcinoma. In addition, there was a deficit of non-NPC pharyngeal cancers, which completely offset the small number of excess NPCs, so that overall there were 17% fewer

pharyngeal cancers observed than expected. The excess may be a statistical aberration , given the deficit for this particular region, and result simply from the multiple comparisons and subdivisions made in the technical report [6].

In a new report [7] published this month from a multi-center case-control study of nasopharyngeal cancer in the United States, no excess risk was found among those occupationally exposed to wood dust, and there were no trends of rising risks with increasing exposure among the exposed.

IARC also looked at lung cancer and did not conclude there was any causal link between wood dust and this endpoint. In the new American cohort study cited earlier [5], 14-17% higher rates of lung cancer were observed, but this small excess was attributed in part to concomitant asbestos exposures, and the authors noted that "no other convincing associations between wood dust exposure or employment in woodworking occupations and the risk of common cancers were observed." Overall, the epidemiologic data on lung and other cancers among woodworkers remain consistent with no effect of wood dust.

References

1. International Agency for Research on Cancer. IARC Monographs on the evaluation of carcinogenic risks to humans, Vol 62, wood dust and formaldehyde. Lyon, France: International Agency for Research on Cancer, 1995.

2. Blot WJ, Chow WH, McLaughlin JK. Wood dust and nasal cancer risk. J Occup Environ Med 1997; 39:148-156.

3. Demers PA, Kogevinas M, Bofetta P, et al. Wood dust and sino-nasal cancer: pooled reanalysis of twelve case-control studies. Am J Ind Med 1995; 28:151-166.

4. Demers PA, Boffetta P, Kogevinas M et al. Pooled reanalysis of cancer mortality among five cohorts of workers in wood-related industries. Scand J Work Environ Health 1995; 21:179-190.

5. Stellman S, Demers PA, Colin D, Boffetta P. Cancer mortality and wood dust exposure among participants in the American Cancer Society Prevention Study II (CPS II). Am J Ind Med 1998; 34:229-237.

6. Demers PA, Boffetta P. Cancer risk from occupational exposure to wood dust. IARC Tech Rpt 30, Lyon, France: International Agency for Research on Cancer, 1998.

7. Vaughan T, Stewart P, Teschke K, et al. Occupational exposure to formaldehyde and wood dust and nasopharyngeal carcinoma. Occup Environ Med 2000; 57:376-384.