

National Estimates of Occupational Exposure to Animal Bladder Tumorigens

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A prevention program for occupational bladder cancer should be based on an estimate of the number of workers previously and currently exposed to bladder carcinogens. The National Occupational Exposure Survey (NOES), which identified potential occupational exposures in approximately 5000 private sector firms in 1981 to 1983, is the best available source for recent hazard estimates; the National Occupational Hazard Survey (NOHS), conducted in 1973 and 1974, for past exposure estimates. The National Institute for Occupational Safety and Health Registry of Toxic Effects of Chemical Substances (RTECS[®]) identified nearly 200 substances associated with animal bladder tumors. From NOES and NOHS, the numbers of workers with full time (≥ 4 hours/day) or any potential occupational exposure were estimated for the United States. About 60 000 workers were potentially exposed in the early 1970s and about 700 000 in the early 1980s on a full-time basis to the compounds on the RTECS[®] list also appearing in NOES, and about 1.8 million workers in the 1970s and almost 3.5 million in the 1980s had some occupational exposure. Because matches were not found for many compounds and because NOES covers only part of the US work force, these are probably underestimates. The estimates for the number of exposed workers do not imply that these workers all have increased risk of developing bladder cancer, because some animal tumorigens may not be human carcinogens and our estimates are based on potential rather than measured exposures. The risk would depend on the potency, duration, and intensity of the actual exposures. Nevertheless these estimates are useful in estimating the approximate magnitude of the potential occupational exposure to animal bladder tumorigens.

Recent studies have estimated that from 21% to 25% of bladder cancers in white men and 27% in non-white men are occupationally related.^{1,2} However, only a small number of high-risk cohorts are under active surveillance and screening for bladder cancer. One step in any discussion of whether screening should be recommended for occupational groups at high risk of bladder cancer is to determine the number of workers who are at potentially increased risk and identify groups that might benefit from screening.

Estimates of numbers of exposed workers can be used for several purposes. First, they clearly assist in understanding the possible magnitude of the public health problem of work-related bladder cancer. Second, they are useful in deciding whether an epidemiologically valid assessment of currently available screening methods is feasible in occupational groups. Third, knowing where exposures might be occurring is crucial for primary prevention efforts. Fourth, knowing where past (10 to 20 years ago) exposures may have occurred points the way to identification of potential high-risk cohorts (some of whose members may have developed bladder cancer already) for which screening programs should be established.

Estimates of the numbers of workers at increased risk of bladder cancer can be derived in two ways. Case-control data can be used to identify occupations and/or industries with excess risk of bladder cancer. Census data can be used to estimate the numbers of workers with these occupations. An alternative approach involves (1) deciding for which chemicals there is sufficient animal or human evidence of bladder carcinogenicity and (2) estimating the number of workers currently exposed to each known or suspected bladder carcinogen. The total of all exposed workers (adjusting for multiple exposures) would be the national estimate.

Both approaches have obvious limitations. The first method, based on case-control study results, often focuses on broad categories, such as "painters," rather

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than more specific measures of occupational exposure and reflects primarily past occupational exposures. The second approach involves the difficulty of deciding whether the scientific evidence is sufficient to designate a specific chemical as a bladder carcinogen. In addition, estimating the number of United States workers exposed to each selected bladder carcinogen is difficult, because there is only a limited number of possible sources of information, and because workers may have multiple exposures, summing the numbers exposed to each chemical would overestimate the total exposed. We selected the second approach because it highlights the use of three National Institute for Occupational Safety and Health (NIOSH) information and surveillance systems: the National Occupational Exposure Survey (NOES), the National Occupational Hazard Survey (NOHS), and the Registry of Toxic Effects of Chemical Substances (RTECS®).

Methods

RTECS®, mandated by the Occupational Safety and Health Act of 1970 (it was then called the Toxic Substances List), is a compilation of published chemical toxicological and related data, updated quarterly.^{3,4} The on-line RTECS® data base was searched to identify any substance associated with bladder tumors. The citations for each compound were reviewed to determine whether there was either at least one scientific study in which exposed animals developed bladder tumors or whether there was substantial human epidemiological evidence for an elevated risk of bladder cancer. About 200 compounds met these criteria.

In addition to the RTECS® search, we conducted a search of other NIOSH sources⁵⁻⁷ to identify dyes based on benzidine, *o*-tolidine, and *o*-dianisidine. Benzidine and benzidine-based dyes are considered by the International Agency for Research on Cancer (IARC) to be carcinogenic or probably carcinogenic to humans and by NIOSH to be potential occupational carcinogens.⁵⁻⁷ There is considerable evidence that benzidine-based dyes pose a hazard in one of three ways: the dye itself may contain benzidine residues, metabolic processes in vivo may liberate benzidine, or the benzidine-based dye itself may be a carcinogen.⁸ Although both *o*-tolidine and *o*-dianisidine are animal carcinogens, the metabolism in vivo of dyes based on these compounds is less well understood than for the benzidine-based dyes. There is some evidence that dyes based on these two compounds could be metabolized to the parent compound.⁸ Several other aromatic amine dyes suspected of being carcinogenic were added to the list.

To estimate the number of workers who might have been exposed recently, NOES was searched for each compound on the lists of dyes and nondyes. To evaluate whether exposures to these chemicals were increasing or decreasing, NOHS was searched for compounds found in the NOES search.

One of the basic objectives of NOES was to derive national estimates of occupational exposures for the

period 1981 to 1983. A stratified random sample of approximately 4500 private sector firms with more than eight employees was surveyed to identify potential occupational exposures. Although no actual industrial hygiene measurements were made, trained surveyors attempted to determine whether some degree of exposure was likely to occur and classified such potential exposure as either full time (>4 hours/day on a daily basis for at least 90% of the company's work year) or part time (>30 minutes/week on an annual average or at least once weekly for 90% of the year's work weeks). To derive national estimates, data from the 4490 firms employing nearly 1.8 million workers are assigned weights based on their inverse inclusion probability: the potential exposure of a single worker in the sample population could be extrapolated to yield a national estimate of as many as 700 potentially exposed workers. Because of these survey features, the estimates are properly described as potential exposure estimates.^{9,10} The National Occupational Hazard Survey (NOHS), a 2-year field study begun in 1972, was "intended to describe the health and safety conditions in the American work environment and, more specifically, to determine the extent of worker exposure to chemical and physical agents."¹¹ The sample of 4636 businesses employing nearly 900 000 workers was representative of all businesses covered by OSHA. Surveys included a management questionnaire about the facility and records of all chemical and physical agents observed in a single walk-through. Agriculture, any mining except oil and gas extraction, rail transportation, facilities with fewer than eight employees, and all government agencies were excluded.

Results

Table 1 presents those RTECS® compounds associated with "bladder tumors," and the scientific evidence for those associations. After the RTECS® list was matched with NOES, an estimation of the quality of the evidence of carcinogenicity of a compound was made for those compounds which matched. All the compounds in Table 1 have been cited in the scientific literature as causing tumors, benign or malignant, in laboratory animals; a small percentage has been cited as causing cancer in humans. The quality and quantity of these studies varies substantially, and most have not undergone critical review. A minority of the positive animal studies have been reviewed by the Environmental Protection Agency (EPA), the National Cancer Institute (NCI), or IARC. On the basis of these reviews, some compounds have been classified by the IARC as group 1 carcinogens, having sufficient evidence of human carcinogenicity (eg, benzidine), group 2A, having limited evidence of human carcinogenicity, group 2B, having sufficient evidence of animal carcinogenicity, or group 3, having limited evidence of animal carcinogenicity.¹² Some compounds have been assessed by NIOSH as potential carcinogens,⁵ some have been rated by the EPA Gene-Tox Program¹³ as *positive: carcinogenicity*-(species name), and some have

TABLE 1
Known and Suspected Bladder Carcinogens*

Compound Name	Evidence of Carcinogenicity		
	EPA	NCI/NTP	IARC
5-Acenaphthenamine			Group 3
Acenaphthene, 5-nitro	+		Group 2B
Acetamide, <i>N</i> -fluoren-2-yl-	+	+	
Acetamide, <i>N</i> -(1-hydroxyfluoren-2-yl)-			
Acetamide, <i>N</i> -(3-hydroxyfluoren-2-yl)-			
Acetamide, <i>N</i> -(4-(5-nitro-2-furyl)-2-thiazolyl)-	+		Group 2B
Acetanilide, 4'-hydroxy-			
Acetanilide, 4'-phenyl-			
Acetic acid, nitrilotri-	+	+	
Acetic acid, nitrilotri- trisodium salt		+	
Acetic acid, (2,4,5-trichlorophenoxy)-	+		Group 2B
Acetohydroxamic acid, <i>N</i> -4-biphenyl-	+		
Acetohydroxamic acid, <i>N</i> -fluoren-2-yl-	+		
<i>p</i> -Acetophenetidide	+	+	Group 2A
Acetophenone, 2-amino-			
Acetophenone, 2'-amino-3'-hydroxy-			
Alanine, 3-(3-hydroxyanthraniloyl)-			
Ammonium (4-bis(<i>p</i> -dimethylamino)phenyl)methylene)-2,5-cyclohexadien-1-yl	+		
Aniline	+		Group 3
Aniline, <i>p</i> -(<i>p</i> -chlorophenoxy)-			
Aniline, <i>N,N</i> -dimethyl- <i>p</i> -phenylazo-	+	+	Group 2B
Aniline, 4,4'-(imidocarbonyl)bis(<i>N,N</i> -dimethyl-, HCl	+		
Aniline, <i>N</i> -methyl- <i>N</i> -nitroso-			
<i>o</i> -Anisidine, HCl	+	+	Group 2B
<i>p</i> -Anisidine, HCl			
<i>o</i> -Anisidine, 5-methyl-	+	+	Group 2B
<i>p</i> -Anisidine, 2-methyl-		+	Group 3
2-Anthracenamine	+		
9,10-Anthracenedione, 1,4,5,8-tetraamino-	+		
Anthranilic acid			Group 3
Anthranilic acid, 3-hydroxy-, methyl ester			
2-Anthrol, 1-(phenylazo)-			
Antipyrine			
Azobenzene, 3,6'-dimethyl			
1,1'-Azonaphthalene			
2,2'-Azonaphthalene			
Benz(a)anthracene	+	+	Group 2A
Benzene, hexaethyl-			
Benzene, hexamethyl-			
Benzidine	+	+	Group 1
Benzidine, 3,3'-dichloro-	+	+	Group 2B
Benzidine, 3,3'-dimethoxy-	+	+	Group 2B
Benzidine, 2,2',5,5'-tetrachloro-			Group 3
Benzisothiazolin-3-one, 1,1-dioxide(saccharin)	+		Group 2B
Benzisothiazolin-3-one, 1,1-dioxide sodium salt (sodium saccharin)	+		Group 2B
Benzoic acid, 2-amino-3-hydroxy-			
<i>p</i> -Benzoquinone, dioxime		+	Group 3
4-Biphenylamine	+		Group 1
4-Biphenylamine, 3,2'-dimethyl-		+	
4-Biphenylamine, 3-methoxy-			
4-Biphenylamine, 4'-nitro-			
Biphenyl, 3,2'-dimethyl-4-nitroso			
3,3'-Biphenyldiol, 4,4'-diamino-			
Biphenyl, 4-nitro	+		Group 3
2-Biphenylol			Group 3
4-Biphenylol, 3-amino-, HCl			
3-Biphenylol, 4-amino-, hydrogen sulfate			
3-Biphenylol, 4-amino-4'-methoxy-, HCl			
3-Biphenylol, 4-amino-4'-nitro-, HCl			
3-Biphenylol, 4-(dimethylamino)-			
2-Biphenylol, sodium salt			Group 2B
Bracken fern			Group 2B

TABLE 1
Cont.

Compound Name	Evidence of Carcinogenicity		
	EPA	NCI/NTP	IARC
Bracken fern tannin			
1-Butanamine, <i>N</i> -butyl- <i>N</i> -nitroso	+	+	Group 2B
1-Butanol, 4-(butylnitrosoamino)-	+		Group 2B
1-Butanol, 4-(ethylnitrosoamino)-			
1-Butanol, 4-(methylnitrosoamino)-			
1-Butanol, 4-(pentylnitrosoamino)-			
1-Butanol, 4-(propylnitrosoamino)-			
Butyric acid, 4-(allylnitrosoamino)-			
Butyric acid, 4-(<i>N</i> -butyl- <i>N</i> -nitrosoamino)-			Group 3
Butyric acid, 4,4'-(3,3'-diamino- <i>p,p'</i> -biphenylenedioxy)di-			
Butyric acid, 4-(ethylnitrosoamino)-			
Butyric acid, 4-(methylnitrosoamino)-			
Carbonic acid, methyl 4-(<i>o</i> -tolylazo)- <i>o</i> -tolyl ester			
Cholesterol			Group 3
<i>p</i> -Cresol, 2,6-di-tert-butyl-	+		Group 3
Cycad husk			
Cyclohexanesulfamic acid			
Cyclohexanesulfamic acid, calcium salt			Group 3
Cyclohexanesulfamic acid, monosodium salt (cyclamate)			Group 3
Cyclohexylamine, sulfate			
Decylamine, <i>N</i> -methyl- <i>N</i> -nitroso-			
Dibenz(a,h)anthracene	+	+	Group 2A
7H-Dibenzo(c,g)carbazole	+		Group 2B
2-Dibenzofuranamine			
3-Dibenzofuranamine			
2-Dibenzofuranamine, 3-methoxy-			
3-Dibenzofuranamine, 2-methoxy-			
Dibenzo(a,c)phenazine			
Dibenzo(a,h)phenazine			
Diethylene glycol			
Dimethylamine, <i>N</i> -nitroso-	+	+	Group 2A
Diphenylamine, <i>N</i> -nitroso-	+	+	Group 3
Dipropylamine, 2,2'-dioxo- <i>N</i> -nitroso-			
Dipropylamine, <i>N</i> -nitroso-	+	+	Group 2B
Dodecylamine, <i>N,N</i> -dimethyl-, HCl mixed with sodium nitrite (7:8)			
Eicosanoic acid			
Estradiol	+	+	Group 2A
Ethanol, 2-(ethylnitrosoamino)-			Group 3
Fibrous glass			
Flavone, 3,3',4',5,7-pentahydroxy-	+		Group 3
Fluoren-2-amine	±		
Formamide, <i>N</i> -(4-(5-nitro-2-furyl)-2-thiazolyl)-	+		
Formic acid, methylhydrazide			
Formic acid, 2-(4-(5-nitro-2-furyl)-2-thiasolyl)hydrazide	+		Group 2B
Gasoline, unleaded			
1- <i>d</i> -Glucosiduronic acid, (2'-aminonaphthyl)-			
Hydroxylamine, <i>O</i> -benzoyl- <i>N</i> -methyl- <i>N</i> -(<i>p</i> -phenylazo)phenyl-			
Hydroxylamine, <i>N</i> -2-naphthyl-	+		
2-Imidazolidinone, 1-(5-nitro-2-thiazolyl)-	+		Group 2B
Indole-3-acrylic acid			
Isothiocyanic acid, allyl ester		+	Group 3
Lactic acid, <i>p</i> -hydroxyphenyl-			
Melamine			Group 3
Methanesulfonic acid, methyl ester	+		Group 3
2,7-Naphthalenedisulfonic acid, 4-amino-3-((4'-((2,4-diaminophenyl)azo)1,1'-biphenyl)-	+	+	Group 2A
2,7-Naphthalenedisulfonic acid, 3,3'-((4,4'-biphenylene)bis(azo))bis(5-amino-	+	+	Group 2A
2,7-Naphthalenedisulfonic acid, 3-hydroxy-4-((2,4,5-trimethylphenyl)azo)-	+		Group 2B

TABLE 1
Cont.

Compound Name	Evidence of Carcinogenicity		
	EPA	NCI/NTP	IARC
Naphthalene, 2-nitro-			
1-Naphthalenesulfonamide, 4-(ethylsulfonyl)-			
2-Naphthalenesulfonic acid, 5,5'-(4,4'-biphenylenebis(azo)bis(6-amino-4-H)			
1-Naphthol, 2-amino-			
2-Naphthol, 1-amino-, HCl			
1-Naphthol, 1-amino-, HCl			
1-Naphthol, 4-amino-, HCl			
1-Naphthol, 2-amino-, phosphate (ester) Na salt			
2-Naphthol, 1-((2,5-dimethoxyphenyl)azo)-	+		Group 2B
2-Naphthol, 1-(phenylazo)-		+	Group 3
2-Naphthol, 1-(o-tolylazo)-	+		Group 2B
2-Naphthol, 1-(2,4-xylylazo)-			Group 3
2-Naphthylamine	+	+	Group 1
2-Naphthylamine, N,N-bis(2-chloroethyl)-	+	+	Group 1
2-Naphthylamine, 1-methoxy-			
2-Naphthylamine, 1-methoxy-, HCl			
2-Naphthylamine, 3-methyl			
19-Nor-17- α -pregna-1,3,5(10)-trien-20-yne-3,17-diol	+	+	Group 2A
Octadecanamide			
1-Octadecanol			
Octane-1-nno-azoxymethane			
Octylamine, N-methyl-N-nitroso-			
2H-1,3,2-Oxazaphosphorine, 2-(bis(2-chloroethyl)amino)tetrahydro-, 2-oxide	+	+	Group 1
Palmitic acid			
Paraffin			
Phenazine			
Phenol, 4-amino-2-nitro-	+	+	Group 3
Phenol, (1,1-dimethylethyl)-4-methoxy-	+		Group 2B
m-Phenylenediamine, 4-chloro-	+		Group 3
o-Phenylenediamine, 4-chloro-	+		Group 2B
Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-N'-(3-hydroxypropyl)-		+	
Polydimethylsiloxane rubber			
1-Propanol, 2,3-dibromo-, phosphate (3:1)	+	+	Group 2A
Propene, 1,3-dichloro-		+	Group 2B
Purine, 6-((1-methyl-4-nitroimidazol-5-yl)thio)-	+	+	Group 1
Pyridine, 2,6'-diamino-3-(phenylazo)-			
5H-Pyrido(4,3-b)indole, 3-amino-1,4-dimethyl-	+		Group 2B
5H-Pyrido(4,3-b)indole, 3-amino-1-methyl-			Group 2B
Pyruvic acid, p-hydroxyphenyl-			
Quinaldic acid, 4,8-dihydroxy-			
Quinaldic acid, 8-hydroxy-			
Quinaldic acid, 4-hydroxy-8-methoxy-			
4-Quinazolinol, 1,2-dihydro-2-(5-nitrofuryl)-, 3-oxide			
4(3H)-Quinazolinone, 1,2-dihydro-2-(5-nitro-2-thienyl)-			
8-Quinololinol			Group 3
Serine, diazoacetate (ester)	+		Group 2B
Silica, crystalline-quartz			Group 2A
Stearic acid			
4-Stilbenamine			
4,4'-stilbenediol, α,α' -diethyl-, dipropionate, (e)-			Group 2B
Sulfuric acid, 2-amino-1-naphthyl ester			
Sulfuric acid, benzidin-3-yl ester			
Symphytum officinale L., leaves			Group 3
Symphytum officinale L., roots			Group 3
Tetradecylamine, N-methyl-N-nitroso-			
Thiazole, 2-amino-4-(5-nitro-2-furyl)-			

TABLE 1
Cont.

Compound Name	Evidence of Carcinogenicity		
	EPA	NCI/NTP	IARC
δ^2 - α -Thiazolidineacetic acid, 4-oxo, butyl ester			
Toluene, 2,4-diamine, dihydrochloride			
Toluene, 2,4-dinitro-			\pm
Toluene, o-nitroso			
o-Toluidine	+	+	Group 2A
o-Toluidine, hydrochloride	+	+	Group 2B
o-Toluidine, 4-(o-tolylazo)-	+		Group 2B
Tryptophan, L-			
Tryptophan, L-, pyrolyzate			
Undecanoic acid, 11-amino-		+	Group 3
Uracil			
Urea, N-methyl-N-nitroso-	+	+	Group 2A
Vincal leukoblastine		+	
Xanthine			
4,5-Xylenol, 2-amino-			

* An RTECS® search for substances associated with "bladder tumors" produced this list of compounds. Notations indicate how compounds were rated by the EPA Gene-Tox Program, NCI/NTP Carcinogenesis Bioassays, and IARC Monographs. Some long compound names have been truncated.

been investigated in carcinogenesis studies conducted by NCI or the National Toxicology Program and given a summary evaluation of *clear evidence: (species name)*. Most of the compounds have not been evaluated by any of these review bodies.

Because there is reason to believe that dyes based on benzidine, o-tolidine (3,3'-dimethylbenzidine), or o-dianisidine (3,3'-dimethoxybenzidine) can be transformed in the body to the parent compound, a search was made^{7,8} for such dyes, and the list of dyes was also matched with NOES and NOHS to obtain estimates of the numbers of workers potentially exposed in the 1970s and 1980s (Table 2). There appears to be a clear trend toward increased exposure to all four classes of dyes from the 1970s to the 1980s.

Results of the NOES and NOHS matches for total number of workers exposed to specific nondyes are presented in Table 3. Occupational exposure to ortho-toluidine, recently associated with significantly increased risk of bladder cancer (E. Ward, A. Carpenter, S. Markowitz et al, unpublished data), increased 88% from the 1970s to the 1980s (Table 3).

NOES and NOHS were searched to categorize, by industry and by occupation, the numbers of persons with exposure to one or more of the potential carcinogens. Table 4 presents the results of those searches by industry; Table 5, by occupation. It should be noted that the estimates of numbers of exposed workers are nonduplicated. That is, each worker is exposed to one or more of the potential occupational carcinogens.

Estimates of the extent of exposure within an industrial or occupational category can be derived by comparing the estimates in Tables 4 and 5 to the NOES or NOHS universe; that is, the estimated number working in the types of facilities sampled. Table 6 makes these

TABLE 2
National Estimates* of Exposures to Aromatic Amine Dyes

Compound Name	Potentially Exposed Workers		
	1980s (NOES)	1970s (NOHS)	Est. % Change
Benzidine-based dyes	28 442†	20 470	+39%
Direct Red 28	4 273	1 518	+180%
Direct Red 10	79	-	
Direct Red 13	3 499	2 799	+25%
Acid Orange 45	47	1 204	-96%
Acid Red 85	220	2 331	-91%
Direct Red 1	830	885	-6%
Direct Blue 2	220	2 174	-90%
Direct Blue 6	3 451	1 328	+160%
Direct Brown 1A	3 499	146	+2 300%
Direct Black 38	10 542	16 418	-36%
Direct Black 4	4 715	-	
Direct Brown 31	830	28	+2 850%
Benzidine	1 554	1 164	+34%
Sulphur Orange 1	177	-	
Direct Brown 95	830	1 106	-25%
<i>o</i> -Dianisidine-based dyes	99 783	16 166	+518%
Pigment Orange 16	42 046	10 858	+290%
Pigment Red 41	1 652	100	+1 550%
Direct Blue 98	21 079	18	+27 000%
<i>o</i> -Dianisidine	2 482	120	+2 050%
<i>o</i> -Dianisidine, dihydrochloride	489	-	
Direct Blue 8	1 450	-	
Direct Blue 15	4 528	68	+6 550%
Direct Blue 1	7 685	1 138	+500%
Direct Blue 218	8 682	2 456	+250%
Direct Blue 80	7 511	1 500	+400%
<i>o</i> -Tolidine-based dyes	60 595	16 377	+270%
Direct Red 2	1 450	-	
Direct Red 39	1 450	2 136	-32%
Acid Red 114	13 795	2 852	+400%
Direct Blue 25	6 004	1 797	+200%
Direct Blue 14	813	-	
Direct Blue 53	5 353	1 753	+200%
<i>o</i> -Tolidine	9 639	418	+2 200%
<i>o</i> -Tolidine, dihydrochloride	1 179	-	
Other dyes	77 568	5 651	+1 270%
Solvent Yellow 14 (monoazo)	43 776	-	
Solvent Orange 7 (monoazo)	774	3 517	-78%
Fourrine Brown PR	11 981	-	
Fast Red BB Base	1 108	-	
Azoic Diazo Component 4	913	-	
Solvent yellow 3 (<i>o</i> -aminoazo-toluene)	1 449	3 810	-62%
Acid Red 26 (monoazo)	1 200	2 140	-54%
Solvent Yellow 2 (monoazo)	1 454	41	+3 450%
Basic Yellow 2 (ketone imine)	14 100	10 099	+40%

* Tables 2-6 contain provisional data as of Jan 1, 1990 from the NIOSH National Occupational Exposure Survey (1981-1983) and National Occupational Hazard Survey (1972-1974).

† Category totals are less than the sum of exposures within categories because a person can be exposed to ≥1 compound.

TABLE 3
Exposure to Known and Suspected Bladder Carcinogens (RTECS/NOES Matches)

Compound Name	Potential Exposed Workers	
	NOES 1980s	NOHS 1970s
Acetamide, <i>N</i> -fluoren-2-yl-	896	-
Acetanilide, 4'-hydroxy-	50 794	9 269
Acetic acid, nitrilotri-	11 749	13 454
Acetic acid, nitrilotri- trisodium salt	9 825	-
<i>p</i> -Acetophenetidine	17 658	4 186

TABLE 3
Cont.

Compound Name	Potential Exposed Workers	
	NOES 1980s	NOHS 1970s
Ammonium, (4-bis(<i>p</i> -dimethyl-amino)phenyl)methylene)-2,5-cyclohexadien-1-yl	64 939	79 824
Aniline	35 789	21 859
Aniline, <i>N,N</i> -dimethyl- <i>p</i> -phenylazo-	1 454	42
Aniline, 4,4'-(imidocarbonyl)bis(<i>N,N</i> -dimethyl-, HCl	14 100	10 114
<i>o</i> -Anisidine, HCl	1 108	-
2-Anthracenamine	298	-
9,10-Anthracenedione, 1,4,5,8-tetraamino-	43 520	482
Anthranilic acid	28	-
Antipyrine	1 765	739
Benz(a)anthracene	28	-
Benzidine	1 554	1 166
Benzidine, 3,3'-dimethoxy-	2 482	122
Benzisothiazolin-3-one, 1,1-dioxide (saccharin)	224 753	44 968
Benzisothiazolin-3-one, 1,1-dioxide sodium salt (sodium saccharin)	57 297	13 433
2-Biphenylol	387 789	221 003
2-Biphenylol, sodium salt	44 652	89 406
Cholesterol	32 763	13 980
<i>p</i> -Cresol, 2,6-di-tert-butyl-	326 646	28 860
Cyclohexanesulfamic acid, monosodium salt (cyclamate)	5 267	83
Diethylene glycol	499 295	273 598
Dimethylamine, <i>N</i> -nitroso-	747	-
Diphenylamine, <i>N</i> -nitroso-	-	3 163
Eicosanoic acid	189	12 080
Estradiol	9 083	2 770
Fibrous glass	282 979	79 301
Gasoline, unleaded	570 057	52 764
Melamine	21 999	31 892
2,7-Naphthalenedisulfonic acid, 3-hydroxy-4-((2,4,5-trimethylphenyl)azo)-	36	827
2,7-Naphthalenedisulfonic acid, 4-amino-3-((4-(2,4-diaminophenyl)azo)(1,1'-bi-phenyl)-	10 542	16 432
2,7-Naphthalenedisulfonic acid, 3,3'-(4,4'-bi-phenylene)bis(azo))bis(5-amino-	3 451	1 333
2-Naphthol, 1-(phenylazo)-	43 776	-
2-Naphthol, 1-(2,4-xylylazo)-	774	3 517
2-Naphthylamine	275	420
19-Nor-17- α -pregna-1,3,5(10)-trien-20-yne-3,17-diol	94	2 770
Octadecanamide	20 584	1 994
1-Octadecanol	172 590	60 590
2H-1,3,2-Oxazaphosphorine, 2-(bis(2-chloroethyl)amino)tetrahydro-, 2-oxide	27 171	-
Palmitic acid	42 672	20 670
Paraffin	506 976	485 821
Phenol, 4-amino-2-nitro-	11 981	-
Phenol, (1,1-dimethylethyl)-4-methoxy-	65 879	4 272
Polydimethylsiloxane rubber	6 511	9 102
Propane, 1,3-dichloro-	1 779	-
Purine, 6-((1-methyl-4-nitroimidazol-5-yl)thio)-	1 848	-
8-Quinolinol	12 432	5 733
Silica, crystalline-quartz	602 019	81 221
Stearic acid	813 782	541 586
<i>o</i> -Toluidine	24 573	13 053
<i>o</i> -Toluidine, hydrochloride	202	-
<i>o</i> -Toluidine, 4-(<i>o</i> -tolylazo)-	1 449	3 811
Tryptophan, L-	17 588	-
Undecanoic acid, 11-amino-	1 532	-
Uracil	1 562	-
Vincalculoblastine	2 137	-
Xanthine	2 545	-

TABLE 4
Exposure by Industry to Known and Suspected Bladder Carcinogens

SIC Codes	Industry	Potential Exposed Workers			
		1980s		1970s	
		Full-time*	Any	Full-time	Any
07-08	Agricultural services, forestry	-	17 173	-	2 862
13	Oil and gas extraction	1 345	34 879	-	6 245
15	General building contractors	3 586	79 027	-	17 267
16	Heavy construction contractors	2 753	51 694	325	6 261
17	Special trade contractors	56 474	287 452	2 784	171 173
19	Ordinance and accessories	-	-	-	2 003
20	Food and kindred products	1 801	52 943	761	25 291
21	Tobacco manufacturers	-	787	227	2 707
22	Textile mill products	40 374	76 884	1 967	11 268
23	Apparel and other textiles	39 674	98 876	-	11 185
24	Lumber and wood products	1 682	35 227	717	6 067
25	Furniture and fixtures	5 065	53 432	163	7 692
26	Paper and allied products	5 809	65 638	2 515	46 464
27	Printing and publishing	11 809	59 334	652	50 774
28	Chemicals and allied products	19 003	114 565	5 658	120 696
29	Petroleum and coal products	6 360	37 615	1 419	18 468
30	Rubber and misc. plastics	42 474	98 670	4 222	49 123
31	Leather and leather products	3 041	11 935	406	6 333
32	Stone, clay, and glass products	29 803	72 394	7 546	55 430
33	Primary metal industries	43 889	97 767	1 117	58 220
34	Fabricated metal products	42 330	131 114	8 282	85 041
35	Machinery, except electrical	49 540	267 371	3 325	87 071
36	Electric and electronic equip.	39 080	121 616	5 944	42 842
37	Transportation equipment	17 218	91 516	1 485	53 491
38	Instruments, related products	9 489	45 576	509	19 539
39	Misc. manufacturing	7 085	28 155	6 826	29 647
40	Railroad transportation	-	1 548	-	-
41	Local and interurban transit	10 907	41 895	-	3 113
42	Trucking and warehousing	1 991	56 785	-	19 505
44	Water transportation	-	11 802	-	4 961
45	Transportation by air	6 517	33 564	-	23 319
46	Pipelines, except natural gas	-	4 190	-	1 399
47	Transportation services	-	86	-	9 868
48	Communication	3 714	37 247	-	28 287
49	Electric, gas, sanitary serv.	742	49 047	-	19 710
50	Wholesale, durable goods	1 215	42 556	2 538	46 321
51	Wholesale, nondurable goods	13 455	43 115	-	-
52	Bldg. materials, farm equip.	-	-	-	1 352
53	Retail general merchandise	-	-	57	41 320
54	Food stores	-	-	-	70 696
55	Auto dealers, service stations	99 560	159 080	-	34 838
56	Apparel and accessory stores	-	-	-	7 130
57	Furn., home furnishings stores	-	-	-	6 190
58	Eating and drinking places	-	-	-	14 354
59	Misc. retail stores	-	-	-	17 531
60-67	Banks, brkrs., insurance, real estate	-	-	-	51 399
70	Hotels and other lodging places	-	-	849	4 250
72	Personal services	4 351	82 216	-	29 265
73	Business services	9 574	77 985	-	31 236
75	Auto repair, serv., garages	5 128	56 225	-	4 146
76	Misc. repair services	336	11 528	-	10 869
79	Amusement and recreat. serv.	-	-	-	16 319
80	Health services	21 165	729 122	84	332 534
84	Museums, botan. gardens, zoos	-	2 310	-	-
89	Misc. services	-	-	-	1 143
Exposed to ≥1 Possible Carcinogen on NOHS-RTECS® match list		658 341	3 471 942	60 379	1 824 214

* Exposure of >4 hours a day.

TABLE 5
Exposure by Occupation

1980 OCC Codes*	Occupation Category	Potential Exposed Workers			
		1980s		1970s	
		Full-time	Any	Full-time	Any
003-037	Exec, administrative, managerial	1 449	24 247	955	173
043-068	Engineers, math and computer science	704	5 531	237	3 574
069-083	Natural science	710	21 795	358	12 757
084-106	Health occupations	3 389	466 685	-	131 694
113-199	Other professions†	2 201	7 581	698	19 241
203-208	Health technologists, technicians	4 929	122 089	67	41 354
213-235	Other technologists, technicians	5 542	73 753	414	21 971
243-285	Sales occupations	-	10 288	19	47 601
303-389	Administrative support, clerical	7 955	85 689	300	124 154
403-469	Service personnel	21 107	311 425	391	271 540
473-499	Farming, forestry, fishing	-	11 314	-	-
503-549	Mechanics, repair, maintenance	17 221	193 011	1 375	171 814
553-599	Construction trades	42 095	306 078	2 777	213 132
613-617	Mining and drilling	122	13 085	-	3 712
633-655	Precision metal workers	32 987	129 258	3 014	56 249
656-699	Precision workers (wood, cloth, etc)	18 137	62 364	57	34 195
703-725	Metal and plastics machine operators	51 754	122 443	9 424	57 389
726-733	Woodworking machine operators	820	20 187	129	1 918
734-737	Printing machine operators	13 450	43 149	-	42 019
738-749	Textile machine operators	63 616	134 971	524	20 289
753-779	Misc. machine operators	108 405	417 048	30 153	301 746
783-785	Fabricators and assemblers	76 443	299 255	3 838	84 631
786-795	Hand workers	2 149	11 638	-	2 530
796-799	Production inspectors, etc	4 489	29 286	1 253	18 832
803-814	Motor vehicle operators†	28 090	115 796	-	22 317
823-834	Other transportation occupations	-	-	-	4 364
843-859	Material moving equipment operators	12 077	46 499	3 362	4 203
863-889	Helpers and laborers	138 488	357 873	1 037*	110 977*

* For comparison purposes, each job title in the NOHS listings (which use 1970 OCC codes) was checked in the 1980 Bureau of the Census index¹⁵ and grouped by its 1980 OCC code.

† Nearly all teaching jobs and a substantial proportion of bus-driving jobs are in the public sector, not covered by NOES or NOHS. Members of many occupational groups work as professional freelancers (lawyers, artists, etc) or independent contractors (truckers, construction trades) and would not be included in either industrial survey.

TABLE 6
Exposure within Selected Occupations

Occupation	1980s			1970s		
	All Workers*	Potentially Exposed Workers		All Workers*	Potentially Exposed Workers	
		Full-time	Any		Full-time	Any
Painters	65 469	-	11 936 (18%)	72 930	-	7 332 (10%)
Machinists	503 074	26 076 (5%)	96 413 (19%)	249 301	856 (.3%)	20 635 (8%)
Truck drivers	471 742	15 793 (3%)	74 396 (16%)	577 563	-	14 896 (3%)
Nurses (RNs)	927 434	2 290 (2%)	410 023 (44%)	472 412	-	113 487 (24%)
Garage workers	156 657	91 444 (58%)	123 386 (80%)	163 337	-	7 172 (4%)
Electricians	251 440	8 645 (3%)	110 645 (44%)	232 208	1 721 (.7%)	88 294 (35%)
Janitors, cleaners	905 291	11 834 (1%)	154 025 (17%)	898 480	280 (.03%)	41 007 (5%)
Assemblers	1 508 060	53 167 (4%)	218 578 (14%)	668 333	3 523 (.5%)	79 262 (12%)
Misc. machine ops	764 768	42 470 (6%)	116 324 (15%)	1 044 354	15 319 (2%)	128 683 (12%)
Machine ops NEC†	517 471	27 492 (5%)	107 809 (21%)	152 611	556 (.4%)	14 591 (10%)
Welders	389 822	23 188 (6%)	79 887 (20%)	328 658	315 (.1%)	4 535 (1%)
Sewing machine ops	817 956	63 616 (8%)	85 175 (10%)	485 913	-	7 375 (2%)
All Workers	19 571 942	658 341 (3%)	3 471 942 (18%)	22 489 817	60 379 (.3%)	1 824 369 (8%)

* NOES denominator data, NOES estimate (all hazard codes) May 25, 1990; NOHS denominator data, Table 52, ref 12.

† NEC, not elsewhere classified.

comparisons for selected occupations. In the three occupations most consistently associated with increased risk of bladder cancer in white men in case-control studies—painters, machinists, and truck drivers¹—the proportion of workers exposed to the potential carcinogens is no greater than in other occupations. On the other hand, some occupations not traditionally associated with increased risk of bladder cancer, such as nurses and electricians, appear to have a substantial proportion of workers exposed, although the proportion of nurses exposed on a full-time basis is lower than the average for all occupations.

For all occupations combined, both the number and proportion of workers exposed to the RTECS[®]-NOES match potential carcinogens, on a full-time or any-exposure basis, appears to have increased from the 1970s to the 1980s.

Discussion

The quantity and scientific quality of the evidence for the carcinogenicity of each compound varied substantially. A feasibility assessment of whether or not bladder cancer incidence or mortality should be studied in a particular occupational group would necessitate a comprehensive review of the studies on which the evidence was based.

We could have expanded our list of potential carcinogens by including compounds structurally similar to known bladder carcinogens, as well as compounds that cause liver tumors in mice and rats, since the pathways for aromatic amine metabolism differ in rodents and humans, and some rodent liver carcinogens have been suspected of being human bladder carcinogens.¹⁴ In addition, some exposures may have been tallied under a variant substance name in NOES or NOHS. For example, NOES includes both "o-toluidine hydrochloride," hazard code W0041, 202 workers; "toluidine, ortho-, hydrochloride," hazard code X8305, 154 workers. For this preliminary study, we did not do an exhaustive check on all possible synonyms for each substance. We also did not check the entire RTECS[®] list directly against NOHS. Therefore, there may be additional substances on the RTECS[®] list but not on the NOES-match list to which workers in the 1970s were exposed.

Because they surveyed sample plants, rather than every plant in an industry, and because surveys could not include all possible hazards, both NOES and NOHS have limitations. The walk-through surveys did not include industrial hygiene measurement of exposures; only one visit was made to each plant sampled, so intermittent exposures could have been missed. All of the estimates are based on extrapolation from a sample, so chemicals not used by any of the firms in the sample would not be included in the data base. Because NOES did not include agriculture, the list also excludes products used in agriculture, such as the pesticide chlorodimeform, considered to be a bladder carcinogen, and its parent compound, 4-chloro-ortho-toluidine.

Nevertheless, these surveys represent unique data sources. Many estimates in scientific and policy literature have been based on data from the 1972 and 1974 NOHS surveys. However, in this report, the later survey conducted between 1981 and 1983 has been used as well, providing both more recent data and the opportunity to assess changes in exposure between the 1970s and 1980s. One of the strengths of NOHS and NOES is that the latter was carefully designed to ensure comparability with the former.

The discordance between the results of this preliminary study and case-control studies in the literature, in terms of occupations considered to be at high risk for bladder cancer, could arise in several ways:

1. We may have included in our list of potential carcinogens a substance to which sizable numbers of workers are exposed but which is not, in fact, a carcinogen for humans.
2. Non-full-time exposure may involve no more exposure than would be received in the environment at large. Workers only occasionally exposed to mixtures containing low levels of substances not confirmed as human bladder carcinogens may not be at any appreciable increased risk.
3. The list is not comprehensive; a major bladder carcinogen may not be on it. This may be why painters, truck drivers, and machinists—usually found to be at increased risk of bladder cancer in case-control studies in white men—do not appear to be more highly exposed than workers in other occupations to the list of compounds.
4. Increased risk of bladder cancer may be due to a risk factor other than an exposure (eg, urinary stasis has been proposed as a risk factor for bladder cancer in truck drivers).
5. The exposures surveyed in NOES occurred in the early 1980s; those in NOHS, in the early 1970s. Workers exposed to a bladder carcinogen 10 to 20 years ago may still be at risk of cancer.

Our study points to some areas that merit future investigation (for example, what is the specific substance(s) responsible for the large number of electricians being included in the exposed group). One of the major values of data bases such as RTECS[®], NOES, and NOHS is the wealth of ideas they provide for future epidemiological studies. We plan to analyze the distribution of industries and occupations substance by substance for our list of potential bladder carcinogens, dyes and nondyes, to focus on the nature of the association between exposures and risks.

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We express our sincere appreciation for the expert advice of Elizabeth Ward, PhD, and to Joseph Seta and Randy Young for their skilled technical assistance in producing the NOES and NOHS output on which the tables are based.

Appendix: Capabilities of the NOHS and NOES Data Bases

The NOHS and NOES data bases associate potential hazards with industry types, occupations, and actual surveyed facilities. The sample of surveyed facilities was designed to permit projections to national statistics based on survey results. It is possible to estimate the total number of people exposed to a particular hazard.

Both NOES and NOHS utilized observational techniques; no environmental measurements were made. Therefore, all data refer to *potential* exposures only. Trademarked products are being resolved into component information; to date this has been accomplished for approximately 70 000 trademarked products in NOHS and 60 000 in NOES. NOHS did not survey agriculture, any mining except oil and gas extraction, rail transportation, facilities with fewer than eight employees, and all government agencies. There were an estimated 22.5 million workers in the NOHS universe; that is, working in the kinds of facilities sampled. NOES did not cover facilities with fewer than eight employees, mining, agriculture, government agencies, financial institutions, wholesale and retail trade, and certain professions. The NOES universe includes approximately 19.6 million workers.

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Erratum

In the article "Blood Gas Analysis as a Determinant of Occupationally Related Disability," by W.K.C. Morgan and George L. Zaldivar (*J Occup Med*. 1990;32:440-443, there is an error in the "Methods" section. On page 441, at the top of the first incomplete paragraph, the sentence should read: "Thus, if the PaO₂ was 60 mm and the PaCO₂ was 30 mm, then the adjusted PaO₂ was 50 mm."