12 Occupational Risk Assessment

Adam M. Finkel
Health Science at the University of Michigan, Ann Arbor, MI, United States

Douglas O. Johns
Spokane Mining Research Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Spokane, WA, United States

Christine Whittaker
Division of Science Integration, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, OH, United States

CONTENTS

LEARNING OBJECTIVES

Students who complete this chapter will be able to

1. Understand the scope, magnitude, distribution, and changes during the past half-century in the major safety and health hazards workers face on the job, both in absolute terms and relative to analogous risks in the community or ambient environment;
2. Become familiar with the institutions (primarily Occupational Safety and Health Administration, National Institute for Occupational Safety and Health, and Mine Safety and Health Administration) set up in the United States to evaluate and control these

DOI: 10.1201/9780429291722-12

hazards and with the major legal, scientific, and political challenges these agencies have faced over the past 50 years;
3. Understand how quantitative risk assessment (QRA) for occupational hazards has developed, how it differs from QRA as applied to similar hazards in the general environment, and which aspects of methodology remain the least well developed; and
4. Appreciate the complex interplay of science and policy involved in controlling occupational risks – in particular, the limited role of formal cost-benefit balancing in managing workplace risks – and be able to discuss some of the innovative approaches government, industry, and labor are contemplating to reduce risks through means other than command-and-control regulation.

BACKGROUND

Just as the nature of work has changed throughout the history of the human species, so too have the health and safety risks to which workers are exposed. Though occupational hazards have long been recognized (for example, there are detailed references in the history of Herodotus, circa 450 BC, to how to safely construct trenches so as to protect workers; even earlier, the Old Testament (Deuteronomy 22:8) instructed the faithful to "make a parapet around your roof so that you may not bring the guilt of bloodshed if someone falls from the roof"), there is little documented evidence of the study of occupational health as a distinct discipline prior to the eighteenth century (Gochfeld 2005). The Industrial Revolution brought with it new and widespread risks of work-related injury, illness, and death, which resulted in organized labor demands and public outcry for better working conditions, ultimately resulting in the passage of laws designed to protect the health and safety of workers (Rosner and Markowitz 2020). Occupational risks have evolved over time, and despite considerable progress in reducing work-related risks in the United States, American workers continue to be exposed daily to persistent and emerging hazards (Schulte 2017; Tamers et al. 2020).

Approximately 60% of the US civilian noninstitutional population ages 16 and over are employed, totaling more than 158 million persons working either full or part time (83.3% and 16.7% of the employed population, respectively) in more than 10 million separate establishments (BLS 2022; US Census Bureau 2022). These people face many of the same hazards on the job as those who do not work full or part time face in their daily lives, including hazards in the ambient environment, the community, the home, and in transportation. As we will see, however, workers almost invariably are exposed to these hazards at a much higher frequency, intensity, or concentration than nonworkers are. In addition, of course, workers are exposed to various unique hazards that are not found outside the occupational setting. A central irony in considering occupational risk assessment in the context of the broad field of risk assessment is that many environmental health standards were motivated by discoveries of human disease in the workplace (see Table 12.1) and are based quantitatively on scientific studies of worker populations. For that matter, quantitative estimates of the value of averting a "statistical fatality" are also derived from economic studies in the workplace (see, e.g., Viscusi 2013) – but too often the protections that have resulted from these inquiries have failed to adequately protect workers. Traditionally, hazards in the ambient environment have captured much greater attention than similar or identical hazards faced to a greater degree by workers.

This chapter focuses on occupational illness, where risk assessment methods have of necessity become relatively well developed, but we need to recognize at the outset that occupational injury was the first workplace problem area to gain national attention. Events such as the Triangle Shirtwaist Fire of 1911, which claimed 146 victims in New York City (Von Drehle 2003), the 1947 explosion in Texas City, in which at least 580 workers died when a docked ship carrying ammonium nitrate exploded (Pandanell 2005), and landmark books such as Upton Sinclair's *The Jungle* ([1906] 1985, detailing working conditions in the meatpacking plants around Chicago) focused some attention on occupational injury events and led finally to the passage of the Occupational Safety and Health (OSH) Act of 1970, which created both the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH). OSHA, along with the Mine Safety and Health Administration (MSHA), which was created by the Federal Mine Safety and Health Act of 1977, is responsible for developing and enforcing workplace regulations and standards. NIOSH, on the other hand, is an agency within the Centers for Disease

Table 12.1: Diseases First Noted in Occupational Settings That Impelled Environmental Standards

Disease	Cause	References
Asbestosis	Asbestos exposure	Selikoff et al. (1965); Selikoff et al. (1967); Selikoff and Greenberg (1991).
Silicosis	Exposure to silica-containing rock dust	For a historical overview, see Bufton and Melling (2005).
Black lung	Exposure to coal mine dust	Black lung disease was recognized in the early part of the 20th century. For an overview of the subject, see Smith (1981).
Byssinosis	Exposure to cotton dust	Corn (1981).
Various malignant and other diseases	Radiation exposure, including radon in mines	For an overview, see Upton (1987).
Lead poisoning	Lead dust exposure	Lead poisoning was known to the ancients; several more recent papers review its effects. See Baker Jr. et al. (1979); Winegar et al. (1977).
Neurological symptoms	Pesticide exposure, solvent exposure	Landrigan et al. (1980); Baker Jr. et al. (1985).
Dermatitis, hyper- pigmentation, keratoses, blackfoot disease	Arsenic exposure	Landrigan et al. (1980).
Leukemia	Benzene exposure	Landrigan (1987).

Control and Prevention (CDC) mandated to conduct occupational health and safety research, train occupational health professionals, and make recommendations for the prevention of work-related injury, illness, and death. While generally considered a nonregulatory agency, NIOSH is directly responsible for the administration of a number of occupational safety and health regulatory programs, including the approval of respiratory equipment and the implementation of the World Trade Center Health Program.

Acute Fatal and Nonfatal Injuries

The most fundamental measure of the risk of occupational fatalities, of course, is the national death toll and the related measure of the death rate. Table 12.2 shows the number of workplace fatalities since the OSH Act was passed more than 50 years ago, along with the number of US civilian employees in each year and the crude death rate (in fatalities per 100,000 workers). Note the current population fatality rate of about 3 per 100,000 per year yields a working-lifetime risk of roughly 1.4×10^{-3} (1 chance in about 750) of suffering a fatal workplace injury during a career. This probability will be put in context later in the chapter when we discuss the various definitions of "acceptable risk" in the workplace and elsewhere.

Figure 12.1.A shows that most of the 4,764 fatalities in 2020 occurred in the construction, transportation, and agricultural sectors of the economy, though as shown in Figure 12.1.B, the fatality rate (per 100,000 workers) is very similar between the construction and mining sectors. Interestingly, total injuries and injury rate are highest in the healthcare and social assistance sectors, as depicted in Figures 12.1.A and 12.1.B, respectively. Figure 12.2 shows general decreases over the past 30 years of the four most frequent work-related fatal and nonfatal events. However,

BOX 12.1 ASSESSING TRENDS IN WORKPLACE POPULATION RISK

Adam M. Finkel

The most striking aspect of these statistics is the rather steady decline in total deaths and the (almost) inevitable decrease in death rate over the 50-year period. Some critics of OSHA (Kniesner and Leeth, 1995) assert that the slope of the downward trend was actually steeper before 1970 than after (which, if true, would not necessarily be an indication of OSHA's ineffectiveness, since we might expect continued decrements in the fatality rate to be harder and harder to achieve as the absolute rate decreased).

Table 12.2: Workplace Fatalities Since the Passage of the OSH Act

Year	Employment Work Deaths Counts	Total Employment (Thousands)	Work Deaths per 100,000 FTE Workers	Employment Work Injury Counts (Private Industry)	Work Injuries per 100 FTE Workers (Private Industry)
1970	13,800	77,700	18.0		
1971	13,700	78,500	17.0		
1972	14,000	81,300	17.0		10.9
1973	14,300	84,300	17.0	6,078,700	11.0
1974	13,500	86,200	16.0	5,915,800	10.4
1975	13,000	85,200	15.0	4,983,100	9.1
1976	12,500	88,100	14.0	5,163,700	9.2
1977	12,900	91,500	14.0	5,460,300	9.3
1978	13,100	95,500	14.0	5,799,400	9.4
1979	13,000	98,300	13.0	6,105,700	9.5
1980	13,200	98,800	13.0	5,605,800	8.7
1981	12,500	99,800	13.0	5,404,400	8.3
1982	11,900	98,800	12.0	4,856,400	7.7
1983	11,700	100,100	12.0	4,854,100	7.6
1984	11,500	104,300	11.0	5,419,700	8.0
1985	11,500	106,400	11.0	5,507,200	7.9
1986	11,100	108,900	10.0	5,629,000	7.9
1987	11,300	111,700	10.0	6,035,900	8.3
1988	10,800	114,300	9.0	6,440,400	8.6
1989	10,400	116,700	9.0	6,576,300	8.6
1990	10,500	117,400	9.0	6,753,000	8.8
1991	9,900	116,400	9.0	6,345,700	8.4
1992	6,217	119,583	5.0	6,799,400	8.9
1993	6,331	120,791	5.0	6,737,400	8.5
1994	6,632	124,469	5.0	6,766,900	8.4
1995	6,275	126,248	5.0	6,575,400	8.1
1996	6,202	127,997	4.8	6,238,900	7.4
1997	6,238	130,810	4.7	6,145,600	7.1
1998	6,055	132,684	4.5	5,922,800	6.7
1999	6,054	134,666	4.5	5,707,200	6.3
2000	5,920	136,377	4.3	5,650,100	6.1
2001[a]	5,915	136,252	4.3	5,215,600	5.7
2002	5,534	137,700	4.0	4,700,600	5.3
2003	5,575	138,928	4.0	4,365,200	5.0
2004	5,764	140,411	4.1	4,257,300	4.8
2005	5,734	142,894	4.0	4,214,200	4.6
2006	5,840	145,501	4.0	4,085,400	4.4
2007	5,657	147,215	3.8	4,002,700	4.2
Year	**Employment Work Deaths Counts**	**Total Hours Worked (millions)**	**Work Deaths Per 100,000 FTE Workers**	**Employment Work Injuries Counts (All Industries)**	**Work Injuries Per 100 FTE Workers (All Industries)**
2008	5,214	271,958	3.7	4,634,100	4.2
2009	4,551	254,771	3.5	4,140,700	3.9
2010	4,690	255,948	3.6	3,883,600	3.8
2011	4,693	258,293	3.5	3,857,700	3.8
2012	4,628	264,374	3.4	3,820,800	3.7
2013	4,585	268,127	3.3	3,753,300	3.5
2014	4,821	272,663	3.4	3,675,800	3.4
2015	4,836	277,470	3.4	3,658,500	3.3
2016	5,190	283,101	3.6	3,534,600	3.2
2017	5,147	285,977	3.5	3,475,900	3.1

(Continued)

Table 12.2: (Continued)

Year	Employment Work Deaths Counts	Total Hours Worked (millions)	Work Deaths Per 100,000 FTE Workers	Employment Work Injuries Counts (All Industries)	Work Injuries Per 100 FTE Workers (All Industries)
2018	5,250	292,528	3.5	3,544,400	3.1
2019	5,333	296,600	3.5	3,496,700	3.0
2020	4,764	269,900	3.4	3,229,200	2.9

Note: Data for injuries and illnesses are first published for survey year 1972. However, due to the lack of a national system for tracking occupational illnesses, it is likely that these numbers reflect solely injuries. In fact, beginning in 1992, the Bureau of Labor Statistics (BLS) reported these data as injuries only and did not mention "illnesses." In 2007, BLS changed its methods for reporting fatality rates and also changed the reporting for injuries from private sector to all sectors. Therefore, caution must be taken in comparing data from before and from after 2007.

[a] *Excludes fatalities from the events of September 11, 2001.*

Sources: *Data from 1970 to 1991 is from National Safety Council Accident Facts, 2022.Data from 1992 to 2020 is from the BLS, 2022. In 1994, the National Safety Council [NSC] changed their reporting method for workplace fatalities and adopted the BLS count. The earlier NSC numbers are based on an estimate; the BLS numbers are based on an actual census.*

within that time span, there have been extended periods in which the trends in these work-related fatalities and injuries have remained flat or even increased.

Table 12.3 provides further detail on the racial composition of workers killed on the job, showing a clear decline in total fatalities and injuries over the past 30 years. However, it is concerning that the death toll has increased among some groups of workers, particularly Hispanics, over the past five to ten years.

For every fatal injury in the United States, nearly 1,000 other nonfatal injuries also occur. In 2020, the BLS reported a total of 2.7 million workplace injuries and illnesses; all but roughly 500,000 of these were injuries; of the illnesses recorded, nearly half were skin conditions or occupational hearing loss, and it is unclear to what extent *any* chronic work-related illnesses such as cancer,

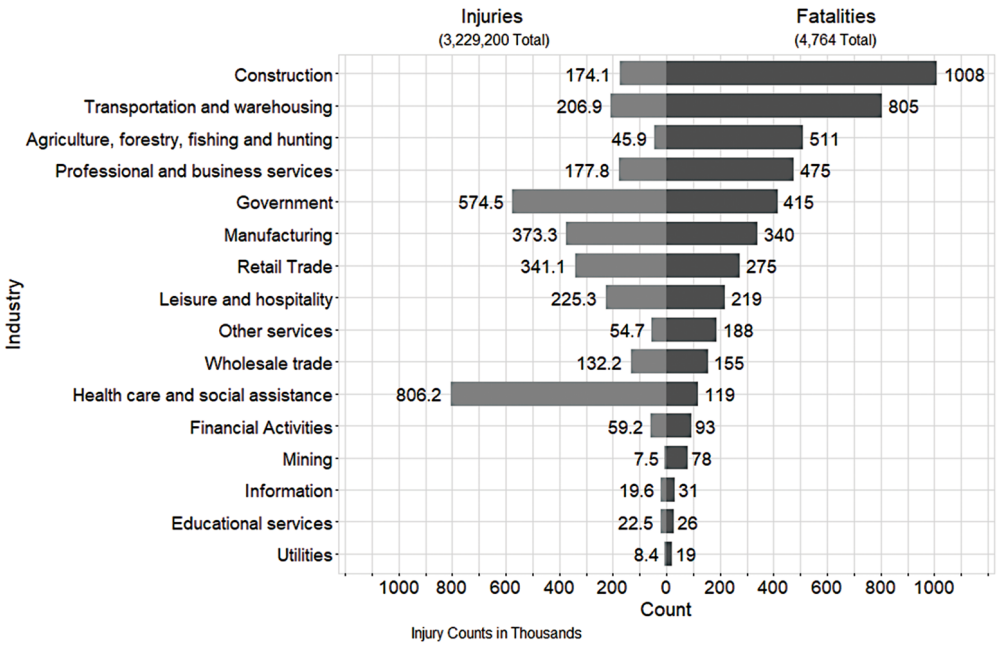

Figure 12.1 (A) Occupational fatalities and nonfatalities by industry, 2020: private sector, government, and self-employment. (Continued)

***Source*: BLS (2020).**

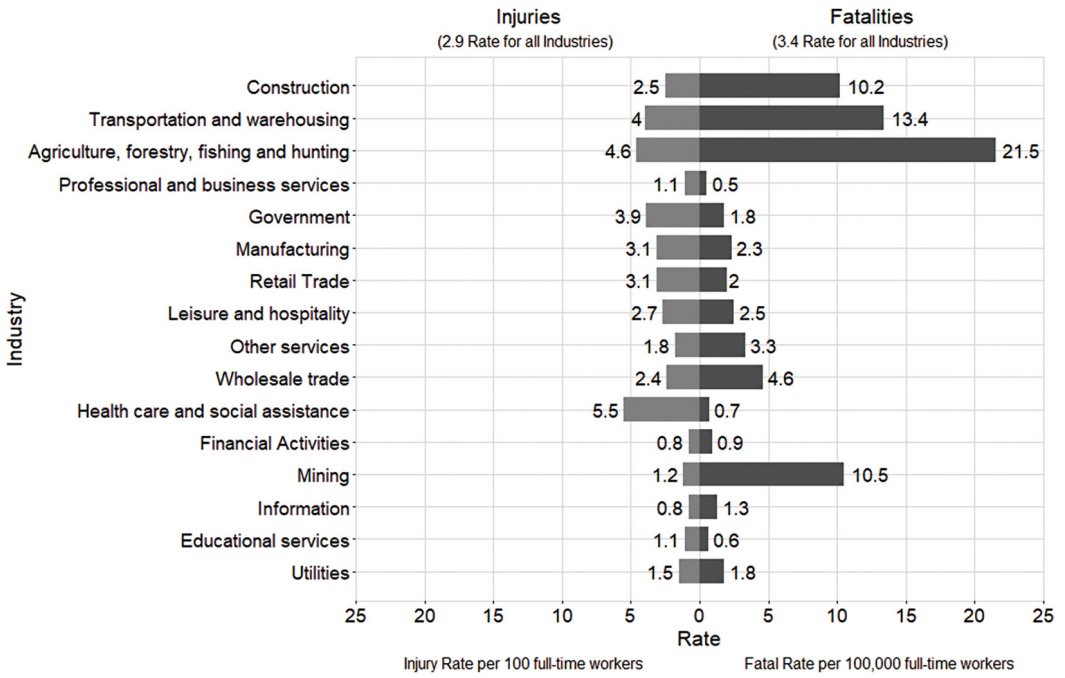

Figure 12.1 (Continued) (B) Occupational fatality and nonfatality rate by industry, 2020: private sector, government, and self-employment.

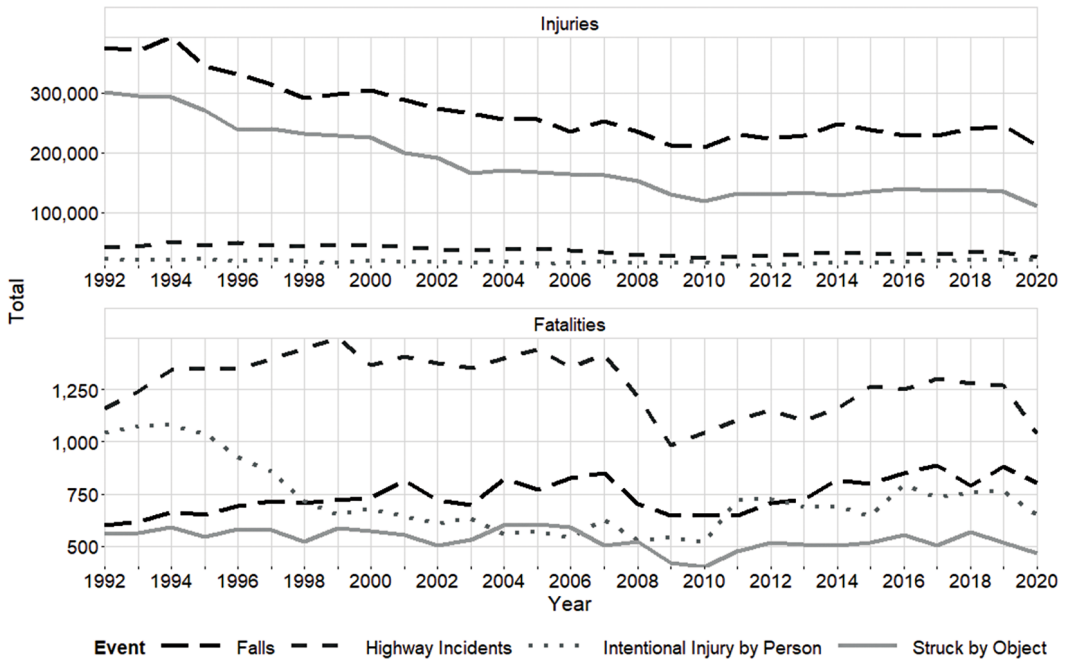

Figure 12.2 The four most frequent work-related fatal and nonfatal events, 1992–2020.

Sources: **Bureau of Labor Statistics (2020).**

Table 12.3: Fatal and Nonfatal Injuries Involving Days Away from Work by Race, 1992–2020

	Total Fatalities	Total Injuries[a]	White		Black or African American		Hispanic or Latino		Asian or Pacific Islander		American Indian or Alaskan Native		Other Races or Not Reported	
			Fatalities	Injuries[a]	Fatalities	Injuries[a]	Fatalities	Injuries[a]	Fatalities	Injuries[a]	Fatalities	Injuries[a]	Fatalities	Injuries[a]
1992	6,217	2,331,098	4,711	1,252,527	618	190,616	533	198,022	169	30,554	36	8,289	150	651,090
1993	6,331	2,252,591	4,665	1,250,071	649	195,780	634	192,304	190	33,230	46	9,156	147	572,051
1994	6,632	2,236,639	4,954	1,234,065	695	197,449	624	189,719	179	33,915	39	7,218	141	574,272
1995	6,275	2,040,929	4,599	1,070,115	684	196,751	619	191,665	161	28,594	27	8,646	185	545,157
1996	6,202	1,880,525	4,586	1,001,424	615	165,700	638	169,300	170	27,010	35	7,316	158	509,775
1997	6,238	1,833,380	4,576	966,289	661	163,823	658	187,221	195	30,969	34	7,551	114	477,528
1998	6,055	1,730,534	4,478	882,428	583	157,435	707	179,399	148	26,782	28	7,431	111	477,058
1999	6,054	1,702,470	4,410	859,591	616	155,149	730	182,896	180	25,328	54	6,812	63	472,693
2000	5,920	1,664,018	4,244	827,455	575	139,280	815	186,028	185	25,857	33	6,955	68	478,442
2001[b]	5,915	1,537,567	4,175	765,228	565	133,785	895	191,959	182	25,317	48	5,661	50	415,616
2002	5,534	1,436,194	3,926	688,009	491	114,453	841	180,419	140	22,099	40	8,225	96	422,989
2003	5,575	1,315,920	3,988	617,160	543	108,470	794	161,330	158	20,400	42	6,910	50	401,770
2004	5,764	1,259,320	4,066	591,570	546	103,820	902	164,920	180	20,690	28	5,140	42	373,180
2005	5,734	1,234,680	3,977	567,790	584	101,170	923	164,600	163	17,950	50	5,830	35	377,480
2006	5,840	1,183,500	4,019	523,320	565	94,370	990	159,440	159	19,170	46	5,190	61	382,020
2007	5,657	1,158,870	3,867	519330	609	94200	937	158,140	172	20,510	29	6130	43	360,560
2008	5,214	1,078,140	3,663	464,500	533	83,970	804	146,800	152	18,010	32	4,230	30	360,630
2009	4,551	964,990	3,204	412,730	421	78,840	713	126,310	148	15,740	33	3,950	32	327,440
2010	4,690	933,200	3,363	391,850	412	73,140	707	123,710	149	14,750	32	4,630	27	325,140
2011	4,693	918,140	3,323	380,740	440	71,740	749	120,340	124	14,730	30	4,340	27	326,260
2012	4,628	918,720	3,177	367,380	486	71,200	748	123,700	154	16,360	37	4,240	26	335,850
2013	4,585	917,090	3,125	363,220	439	70,500	817	125,270	132	15,190	35	4,850	37	338,100
2014	4,821	916,440	3,332	358,210	475	72,280	804	125,250	142	17,390	34	4,020	34	339,300
2015	4,836	902,160	3,241	347,200	495	73,590	903	125,820	123	17,020	36	4,040	38	334,500
2016	5,190	892,270	3,481	325,760	587	73,460	879	128,630	167	15,680	38	3,900	38	344,850
2017	5,147	882,730	3,449	308,610	530	69,900	903	123,510	161	15,870	38	3,640	66	361,230
2018	5,250	900,380	3,405	298,030	615	71,600	961	124,450	163	15,050	42	3,270	64	388,000
2019	5,333	888,220	3,297	295,340	634	73,930	1,088	125,160	195	15,120	30	3,110	89	375,600
2020	4,764	1,176,340	2,898	367,280	541	106,730	1,072	161,890	158	25,290	32	4,130	63	511,030

[a] Injury counts based on the number of nonfatal occupational injuries involving days away from work by selected worker characteristics and number of days away from work, and median number of days away from work, private industry, 1992–2020.
[b] Data from 2001 exclude fatalities from September 11, 2001, terrorist attacks.
Source: BLS (2022).

heart disease, or neurological damage are recorded. The injury rate for the entire population was roughly 4.8 cases per 100 workers in 2004, with rates of 10 per 100 or more (that is, 1 chance in 10 of being injured during the year) in especially risky occupations such as primary metal manufacturing, wood products manufacturing, air transportation, courier services, and nursing home care. More than half of the injuries in 2004 were serious enough to involve one or more days away from work and/or a change of working conditions (i.e., transfer to a different job or restrictions placed on work activities) dictated by the injury; nearly 25% of these lost-workday injuries were serious enough to result in one month or more of an absence from work.

Work-related fatalities can be enumerated rather precisely, with the annual number of deaths attributable to occupational injuries in the United States placed in the 5,000 to 8,000 range (Pratt et al. 1996; Stout and Linn 2002). The national recording systems doubtless fail to count some nonfatal injuries occurring at work, either because of exemptions to the required reporting or the failure of some employers to file reports. A recent article (Rosenman et al. 2006) found that the BLS data accounted for only about 32% of work-related injuries that occurred in Michigan during 1999–2001, suggesting a substantial underestimate.

Occupational Disease

The total number of deaths attributed to occupational exposures is more difficult to quantify. Inspection of Table 12.1 reveals the potential for numerous occupationally related diseases. Research in this area often focuses on a single disease or a single industry; compendia of data are not available. However, the number is certainly much greater than the numbers for injury fatalities. Neurodegenerative diseases, lung diseases, and various forms of cancer suggest a much higher total likely in the 50,000 to 75,000 deaths-per-year range. The true numbers may be even higher since the effects of occupational exposures to physical and chemical stressors are not completely understood. Perhaps the most sophisticated estimates of the number of occupational diseases in the United States were derived by Leigh et al. (1997), who developed an estimate of "the incidence, the mortality, and direct and indirect costs associated with occupational injuries and illnesses in the United States" for the year 1992 using a complex methodology (see also Takala et al. (2014) for similar estimates worldwide and more recent estimates for the United States). They took data from several government agencies and made use of an attributable risk proportion argument whereby the fraction of risk directly attributable to occupational exposures is applied to general morbidity and mortality statistics. They estimated that roughly 60,000 deaths and 850,000 illnesses annually can be attributed to chronic diseases caused by workplace exposures.

BOX 12.2 OCCUPATIONAL SAFETY *OR* HEALTH? RESOURCE ALLOCATION AT OSHA

Adam M. Finkel

In comparing the magnitude of the national problem of fatal occupational injuries with that of premature deaths due to occupational disease, there is no doubt that the latter number is far greater than the former. As many as ten times more workers die prematurely from occupational disease than from acute occupational injury, as evidenced by the previously cited studies and the galvanizing examples of worker disease in the past (e.g., Hawk's Nest, black lung, brown lung, and vinyl chloride; see Cherniack 1986; Young Jr. and Rachal 1996; Annas 1981; Jones 1981). Nevertheless, OSHA continues to devote a very large and arguably a growing per centage of its staff, budget, and enforcement resources to the problem of worker injury. OSHA claims (Cordaro 2015) that roughly 20% of its inspections are "health inspections," implying that while inspections looking for safety violations dominate, a substantial minority of OSHA inspections are designed to find and fix chronic disease hazards. However, it turns out that OSHA tallies as a "health inspection" any investigation where the lead inspector is an industrial hygienist, even if the inspection involves no chemical sampling or attempts to find violations of OSHA health standards. Finkel (2008) testified that based on OSHA's own affidavits in a Freedom of Information Act case he litigated, only about 3% of OSHA's inspections involve any air, wipe, or bulk chemical sampling. Examination of the complete data file for OSHA sampling in the calendar year 2019 (OSHA 2019) reveals that samples were taken at 2,093 unique establishments; this figure indeed represents 2.7% of the 75,463 inspections (federal OSHA plus all state-plan states) conducted in that year.

Occupational Exposures

Unfortunately, it is virtually impossible to produce a predictive (as opposed to the epidemiology-based estimates discussed earlier in the chapter) estimate of the aggregate risk of occupational exposures to toxic substances due to a lack of historical measurements of exposures in workplaces. There has never been a comprehensive survey of what substances US workers are exposed to and at what concentrations. Two attempts to survey a representative sample of workplaces for certain substances were carried out by NIOSH in the mid- to late-1980s: a 1983 study of exposure measurements in approximately 4,500 workplaces in over 500 industries and an analogous mining-specific 1989 study in 431 metal-nonmetal mines and 60 coal mines. Since 1989, though, the CDC has conducted nearly 20 separate National Health and Nutrition Examination Surveys (NHANES) to gauge the nutritional status of US residents, several of which have included extensive survey questions to estimate exposures to chemicals in the home and extensive measurements of the body burdens (i.e., the total amount in the body) of various substances in residents.

The largest database of nonrandom samples of contaminant concentrations in US workplaces is the result of OSHA compliance inspections (note that while some observers insist that because these samples are taken during inspections, they are biased high, toward facilities with the worst concentrations, it is also quite possible that because OSHA often conducts its sampling only as incidental to safety-focused inspections, these readings are not systematically biased). Since 1979, when the agency began collecting inspection information in a single database, OSHA inspectors have collected more than two million air, wipe, and bulk samples. OSHA has never published reports analyzing trends in these data, and only a handful of journal articles have done so for various single substances (Gomez 1991; Lavoue et al. 2013; Yassin et al. 2005). These data are now available on a public website (https://www.osha.gov/opengov/health-samples), allowing access to and searches among these data.

Another source of occupational chemical exposure data is the NIOSH Health Hazard Evaluations (https://www2a.cdc.gov/hhe/search.asp), which summarize NIOSH investigations at individual facilities and often include measured exposure data. However, these data sources are not comprehensive, and thus even the most basic questions about the average contaminant levels workers are exposed to across multiple establishments can only be roughly estimated. It is worth noting that a preliminary investigation concludes that for some substances, workers face concentrations up to one *millionfold* higher than citizens face in the ambient environment (Finkel 2005).

With regard to *criteria pollutants*, occupational settings typically display higher concentrations of airborne pollutants than are allowed in communities or ambient air, but perhaps not on the order of 3 to 6 orders of magnitude that are seen in the case of toxic air pollutants. Table 12.4 compares the allowable values for several air contaminants. *Permissible exposure limits* (PELs) are occupational standards OSHA sets that supply a degree of protection for workers exposed to such compounds in their work environments. They represent time-weighted, eight-hour exposure levels. For example, in the case of sulfur dioxide, a worker could be exposed to 5 ppm of SO_2 for an entire eight-hour shift without a violation of the PEL. Similarly, a worker could be exposed to 10 ppm for four

Table 12.4: A Comparison of Occupational Standards and Ambient Air Quality Standards

Compound	PEL[a]	NAAQS[b]	Notes[c]
NO_2	5 ppm[d]	100 ppb	1-hour average
SO2	5 ppm	75 ppb	1-hour average
O_3	0.1 ppm	0.07 ppm	8-hour average
CO	50 ppm	9 and 35 ppm	8-hour and 1-hour averages
Lead	0.05 mg/m^3	0.00015 g/m^3	Quarterly average[e]
Dust	15 mg/m^3	0.035 and 0.012 mg/m^3	24-hour and annual averages[f]

[a] *Permissible exposure limit (PEL)*: eight-hour time-weighted average allowed values in occupational settings.
[b] *National ambient air quality standards (NAAQS)*: allowable outdoor concentrations; designed to protect health and supply a margin of safety.
[c] NAAQS often have multiple standards with different averaging times for the same contaminant. The longer the averaging time, the lower the allowed concentration.
[d] The OSHA PEL for NO_2 is a ceiling limit not to be exceeded at any time.
[e] Rarely violated since the removal of lead from gasoline.
[f] NAAQS listed for $PM_{2.5}$.

hours, and there would be no violation of the standard if no further exposure were experienced during the eight-hour shift. Note that for some substances, OSHA establishes short-term limits (STEL) not to be exceeded over a short averaging time (typically 15 minutes) or ceiling limits that cannot be exceeded for any length of time. National Ambient Air Quality Standards set by EPA are generally much lower than PELs, as they are required to protect the general population (including sensitive subpopulations) and supply an adequate margin of safety for such individuals. Note that Table 12.4 involves a comparison of regulatory limits, whereas the preceding discussion of toxic air pollutants involves a comparison of measured or modeled concentration values – therefore, the ratios of occupational to environmental values must be interpreted separately in light of the different sorts of comparisons being made here.

An exception to this general trend is found for ozone exposure. Allow able ozone exposure in the occupational environment does not differ substantially from what is allowable in the

BOX 12.3 ASBESTOS IN THE WORKPLACE

Jeffery Mandel

"Asbestos" is the name given to a group of six different fibrous silicates, five of which are considered amphiboles (amosite, crocidolite, tremolite, actinolite, anthophyllite) and one belongs to the serpentine family of minerals (chrysotile). All of these minerals occur naturally in the environment and have found their way into a multitude of manufacturing processes because of their inert properties, particularly as heat insulators and fire protectors. Each type may exist in fibrous (asbestiform) and non-fibrous forms, depending on their ability to cleave along parallel planes (fibrous). The ability to cleave results in greater exposure and pathogenicity. As a rule, the amphibole types are considered more pathogenic, although all types have the potential to cause respiratory disease. Currently, chrysotile is the predominant mineral fiber in use and is still mined and used legally in some countries.

Generally, the amphibole types are longer and thinner, with dimensional characteristics typically greater than 5 microns in length and 0.25 microns in width. Toxicity in humans is related to these fiber dimensions, likely due to the inability of the immune system (e.g., macrophages) to clear these fibers. The pathogenicity is also related to the ability of the fiber to penetrate into the deeper parts of the lungs, the concentration of exposure and the length of time exposed. These factors result in an accumulation of fibers and subsequently increased risk for lung pathology. Shorter and thicker fibers are considered less pathogenic. Non-fibrous, shorter fibers are considerably less pathogenic.

In terms of human disease, excessive fibrous exposure primarily results in lung disease characterized by one or more of the following: plaque (scarring) formation around the lining of the lungs, fibrous scarring of the lung substance (pneumoconiosis), lung cancer (all types) and mesothelioma, a rare cancer of the mesothelial lining surrounding the lungs. This same risk of smoking does not apply to mesothelioma. As a general rule, the lung cancer risk associated with fibrous asbestos exposure is in the range of four to five times higher than those not exposed. In the presence of heavy cigarette smoking and fibrous asbestos exposure, the risk of lung cancer increases in a multiplicative way. Fibrous asbestos-related diseases are all related to the amount and length of exposure and, typically, require a prolonged latency before the disease manifests.

For regulatory purposes, the time-weighted average (TWA) that has been adopted by OSHA for fibrous asbestos is 0.1 fibers per cubic centimeter of air. The TWA is used in combination with the length of exposure in years to provide a cumulative exposure estimate. OSHA also uses the aspect ratio (length:width ratio) greater than 3:1 for counting significant fibers. Specific microscopic methods are employed to make this measurement, including phase contrast and transmission electron microscopy. As a point of reference, cumulative occupational exposure to the above metrics, in the range of 5–1,200 fiber years per cubic centimeter has resulted in pneumoconiosis and lung cancer. Exposure to fibrous asbestos also occurs to the GI tract. Accordingly, concern has been expressed for the development (and risk) for GI cancers to occur in the setting of this exposure. However, epidemiologic investigation into non-respiratory cancer risk has not been definitive.

community, since health effects are found at only modestly elevated concentrations of this irritating air contaminant.

Together, all these injuries (fatal and nonfatal) and illnesses exact a huge cost on the nation, albeit one that is hard to estimate or even to define precisely. In particular, less severe impairment – ranging from minor hearing loss to full disability – increases the social cost of occupational disease substantially (Leigh et al. 2004). Considering only some of these costs (e.g., medical expenses and lost earnings) and explicitly ignoring other costs that are even harder to quantify (e.g., pain and suffering and effects on the families of the victims), Leigh et al. (1997) estimated that occupational injuries and illnesses cost approximately $171 billion annually (roughly 2% of the entire US gross domestic product). A report by Islam and Anderson (2006) estimated the cost of work-related injuries and disease to be $176 billion annually in the United States.

Controlling exposures to workplace hazards also involves substantial costs, although the amount already spent on the controls that currently exist may bear no relationship to the amount that would be needed to avert the injuries and illnesses that still occur. One such cost estimate comes from Johnson (2001), who estimated that OSHA regulations cost the economy roughly $40 billion annually. However, evidence supports the view that the costs of occupational regulations are generally overestimated, partly due to economies of scale or technological learning after promulgation. In the workplace, the most comprehensive study (OTA 1995) suggested that costs predicted before regulations are implemented often exceed actual costs by a factor of two or more; a more recent study found even greater bias (Ruttenberg 2004). A well-known case example is OSHA's vinyl chloride regulation, where dire predictions of oppressive costs evaporated within weeks of the final issuance of the standard; it turned out that reducing workplace concentrations of vinyl chloride also *saved* companies money, as they wasted less of the valuable product into the atmosphere (Chemical Week 1976).

Assessing and Managing Workplace Risks: NIOSH, OSHA, and EPA

NIOSH

Research and Recommendations. NIOSH is organized into divisions, laboratories, and offices located throughout the United States covering a broad range of research and programmatic areas, including occupational health and safety surveillance, exposure assessment, workplace health and hazard assessments, laboratory and basic etiological research, and control of workplace hazards, among others. Integrating findings from these efforts, NIOSH conducts qualitative and quantitative occupational risk assessments, develops policy and technical documents, and develops and disseminates educational occupational safety and health information. Through the OSH Act, NIOSH has the authority to recommend occupational health and safety standards to protect workers from toxic substances and physical agents that are "safe for various periods of employment, including but not limited to the exposure levels at which no employee will suffer impaired health or functional capacity or diminished life expectancy as a result of [their] work experience" (Pub. L. 91-596, Sec 20(a)(3)). Such recommended exposure limits (RELs) are typically published in criteria documents and finalized in response to internal and external peer reviews and public comments.

In addition to criteria documents, NIOSH develops and publishes guidance on assessing risks to workers. Two notable documents of relevance to this discussion are the *NIOSH Chemical Carcinogen Policy* (2016a) and *NIOSH Practices in Occupational Risk Assessment* (2020). The first document describes how NIOSH classifies chemical carcinogens in the workplace, sets a target risk for occupational carcinogen risk assessments of 1 excess cancer case per 10,000 workers exposed to a carcinogen over a working lifetime, and describes how NIOSH considers the ability to detect and quantify airborne concentrations of chemicals in developing its guidance. The second document provides guidance on how NIOSH conducts occupational risk assessments and includes information on data selection, hazard identification, exposure-response modeling methods, use of uncertainty factors, and other topics related to occupational risk assessment.

OSHA

Regulation and Enforcement. OSHA is the federal agency responsible for promulgating and enforcing regulations to protect US workers from hazards that cause injuries and disease. Counting both those employed by the federal agency and those who work for the roughly 25 state OSH agencies that conduct their own inspections, OSHA employs roughly 1,800 inspectors, responsible for over 10 million establishments. These inspectors, called "CSHOs" for "compliance safety and health officers," visit worksites and look for violations of specific OSHA safety and health standards or breaches of the "general duty clause" of the OSH Act, which allows OSHA

to issue citations against employers who knowingly fail to abate "recognized hazards that are causing or are likely to cause death or serious physical harm" (even in the absence of a specific standard). In 2021, federal OSHA conducted about 24,300 inspections, and the state agencies with delegated authority conducted about 31,000 more: roughly one-third of these were programmed inspections of companies whose injury rates the previous year were among the highest in the nation. Roughly one-quarter of the inspections were in response to complaints filed by employees, or to accidents that caused fatalities or multiple hospitalizations, and roughly one-quarter were in response to referrals from other local, state, or federal organizations or follow-up inspections to verify satisfactory abatement of hazards previously identified. Nearly 60% of all inspections now involve construction sites, although that percentage may appear higher than expected because OSHA records multiple inspections at the same construction site when it examines the work of different contractors.

When OSHA inspectors find violations at the worksite, they can recommend various levels of monetary penalty; about 60% of all violations are deemed *serious*, meaning that they cause a substantial probability of death or serious physical harm, with an average penalty of roughly $3,000 per violation (generally, most OSHA penalties are negotiated downward by 50% or more during discussions with employers). Another 3% are repeat violations of the same standard by the same employer (roughly $13,000 average penalty), and about 0.5% are *willful*, meaning that they are committed knowingly by an employer who either intentionally disregards the standard or is "plainly indifferent to its requirements," with an average penalty of $60,000. A Pulitzer prize-winning series in the *New York Times* (Barstow 2003) documented that although over 1,200 cases between 1982 and 2002 involved willful violations that had led to worker deaths, OSHA sought criminal charges against the employers in only about 80 of those cases (7%).

If OSHA was provided the personnel and budget to conduct more on-site inspections, recent scholarship indicates that inspections are not only a way to recognize (and, it is hoped, avert) dangerous workplace conditions, but that they have a significant, lasting, and economically reasonable effect on reducing worker injuries themselves. Writing in the journal *Science*, researchers from the business schools at Berkeley and Harvard (Levine et al. 2012) found that establishments in California that Cal/OSHA randomly chose for inspection saw their workplace injury rate decline by almost 10% more than a matched group of California firms that were not inspected. The researchers concluded that this harm reduction persisted for at least five years after the initial inspections and that the inspected firms experienced no measurable declines in sales, employment, or credit rating.

The OSH Act empowers OSHA to set mandatory standards to govern specific safety and health risks. Congress gave OSHA special authority during the first two years of the agency's existence (1970–1972) to "inherit" existing national consensus standards such as those developed by the American National Standards Institute (ANSI), the American Society for Testing and Materials, the National Fire Protection Association, and other organizations, as well as those that were issued under the Walsh-Healey Public Contracts Act of 1936, and adopt them as mandatory regulations. Also, during this period, OSHA adopted roughly 400 threshold limit values (TLVs®) that had been recommended before 1968 by the American Conference of Governmental Industrial Hygienists (ACGIH), establishing them as mandatory PELs. Since 1972, however, OSHA has had to promulgate standards under a lengthy (and increasingly complex) process. Due to the lengthy and complex nature of the standard-setting process and the small number of staff assigned to develop standards, OSHA has only promulgated about 40 safety standards and 25 health standards since 1972. For only 18 substances (see Table 12.5) has OSHA established mandatory exposure limits and only roughly half of those were based on risk assessment. Two of OSHA's most far-reaching standards were promulgated but never took effect. In 1989, OSHA attempted to modernize its list of over 400 PELs to keep up with changes (almost exclusively more stringent changes) to the TLVs between 1970 and that date. A federal judge invalidated the new list, however, on the grounds that OSHA had failed to undertake any of the quantitative risk assessment (QRS) the Supreme Court had deemed essential in the 1980 *Benzene* decision (see p. 242). In 2001, in the first use of the 1996 Congressional Review Act, both houses of Congress repealed OSHA's new ergonomics standard that would have required controls to reduce repetitive stress injuries at work.

Role of the EPA in Occupational Risk Management

While the primary role of the EPA has focused on the protection of the health of individuals in the community setting, the agency has also been involved periodically with occupational health protection from chemical exposures.

Table 12.5: Substances with a Permissible Exposure Limit Set by OSHA Since 1971

Substance	Year Final Standard Issued (after Subsequent Revisions, if Any)
Vinyl chloride	1974
Coke oven emissions	1976
Dibromochloropropane	1978
Arsenic	1978
Cotton dust	1978
Acrylonitrile	1978
Lead	1978 (general industry); 1993 (construction)
Ethylene oxide	1984
Benzene	1987
4,4′-Methylenedianiline	1992
Cadmium	1992
Formaldehyde	1992
Asbestos	1992
1,3-Butadiene	1996
Methylene chloride	1997
Chromium (hexavalent)	2006
Respirable Crystalline Silica	2016
Beryllium	2017

Toxic Substances Control Act. The Toxic Substances Control Act (TSCA) of 1976 provided EPA with the authority to require reporting, record keeping, testing, and restrictions relating to chemical substances and mixtures. TSCA applies to almost all chemicals in the environment with the exception of food, drugs, cosmetics, and pesticides, which are covered under different laws. Under TSCA, EPA has the authority to

- require premanufacture notification for new chemical substances before manufacture;
- require testing of chemicals by manufacturers, importers, and processors;
- issue Significant New Use Rules (SNUR) when a significant new use was identified that could result in exposures or releases of concern;
- maintain an inventory of existing chemicals;
- require certification of importing and exporting of chemicals;
- require record keeping and reporting by manufacturers, importers, processers, and distributors of chemicals; and
- require manufacturers, importers, processors, and distributors of chemicals to immediately report to EPA information that reasonably supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.

Although EPA's focus was typically on community and environmental exposures to chemicals, in implementing the new chemical provisions of TSCA, EPA frequently assessed risks to workers during the premanufacture and SNUR evaluations. This is in contrast to how EPA typically handled existing chemicals, where EPA focused almost exclusively on community and environmental exposures.

On June 22, 2016, the first major update to TSCA was signed into law. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the TSCA. This update had far-reaching implications for how EPA assesses and regulates both new chemicals and existing chemicals. Some of the major updates include

- a requirement for EPA to evaluate existing chemicals with clear and enforceable deadlines,
- comprehensive risk evaluations for existing chemicals,

- increased public transparency for chemical information, and
- a consistent source of funding for EPA to implement the provisions of the law.

The most impactful change with regard to occupational risk assessment was the addition of workers to EPA's scope. In the definitions, Sec.3 (12) is the following:

> The term "potentially exposed or susceptible subpopulation" means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, ***workers,*** or the elderly.

This addition expanded EPA's role in evaluating workers' risks beyond consideration of new chemicals to risks from exposure to existing chemicals. In its risk evaluation under the amended TSCA, EPA determines whether substances present an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors. This includes a determination of unreasonable risks to potentially exposed or susceptible populations, such as workers. EPA has not defined specific risk probabilities that are identified as unreasonable risk because they determined that it would be "inappropriate to capture the broad set of health and environmental risk measures and information that might be relevant to chemical substances." Instead, EPA considers specific factors that the agency uses in making its risk determinations. According to the EPA *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, these factors include

- the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and noncancer risks),
- the effects of the chemical substance on the environment and environmental exposure under the conditions of use,
- the population exposed (including any susceptible populations),
- the severity of hazard (the nature of the hazard, the irreversibility of hazard), and uncertainties.

For carcinogens, the risk probability EPA considers unreasonable is becoming clearer. As of this writing, several TSCA risk evaluations have now been finalized, and for carcinogenic hazards, EPA has repeatedly cited the *NIOSH Chemical Carcinogen Policy* target risk level of 1 excess cancer case per 10,000 workers exposed to a carcinogen over a working lifetime as its guidance for *unreasonable risk*. When EPA determines that exposures may lead to unreasonable risk, the agency is required to develop risk mitigation strategies to eliminate those risks. These may include banning the chemical; development of restrictions on handling and use, including implementation of engineering controls, work practices, and selection and use of personal protective equipment; and development of occupational (or environmental) exposure limits.

While TSCA confers broad authority to EPA to conduct occupational risk assessment and develop chemical regulations for the workplace, it is not the only statutory authority that EPA has that impacts worker health.

Development of Acute Exposure Guidelines. EPA has an ongoing program designed to assess risks and develop guidelines for short-term or *acute* exposure to environmental contaminants. These Acute Exposure Guideline Levels (AEGLs; Environmental Protection Agency 2006a) focus on exposures that occur very infrequently, and that might be caused by a spill, a train crash, or another catastrophic event. According to EPA (2006a), AEGLs are threshold exposure limits for airborne contaminants applicable to the general public that occur over acute time scales, usually defined as ten minutes to eight hours. Such exposures are likely to produce toxic effects. Airborne concentrations below the AEGL-1 represent exposure levels that can produce mild and progressively increasing, but transient and nondisabling, effects. AEGL-1 levels are airborne concentrations above which most individuals, including sensitive individuals, are likely to experience discomfort but which are transient and not likely to disable the individual. The next level, AEGL-2, may result in long-lasting or permanent effects and may result in impairing the individual's ability to escape from the exposure. The highest AEGL is AEGL-3, a level that, if exceeded, is likely to cause life-threatening effects or even death. While AEGLs are written to apply to all members of the public, workers, such as first responders, are most likely to experience such exposures and are at higher risk because of this.

It is of interest to examine how such standards are developed. In developing AEGLs, EPA works with both national authorities, such as OSHA, and local authorities, including county public health offices. Typically, EPA makes use of a Federal Advisory Committee (2006) that consists of scientists, physicians, and stakeholders drawn from the community at large and who act as special government employees in developing these standards for exposure. The process is iterative, with reviews by two different external committees before the final AEGL is finalized, with the National Academies serving as the final peer reviewer. As can be seen from this development, the AEGL process is designed to afford input from many different groups of scientists and stakeholders in developing these important standards. Further, the iterative process ensures that up-to-date information from the published literature as well as ancillary information from other sources is used to afford protections to those likely to be exposed. However, we hasten to emphasize that the public process for developing OSHA standards and NIOSH recommendations is also quite rigorous. In addition to all of the opportunities for public written and oral comment during public meetings on the topic, OSHA is unusual among federal agencies in that it is required to conduct rulemaking hearings in which OSHA staff are made available for cross-examination by members of the public and the regulated communities. Also, OSHA and EPA are two of the three federal agencies (the Consumer Financial Protection Bureau being the third) that must conduct a separate round of comment before it proposes a regulation, limited to representatives from the small business community who were given special access via the 1996 Small Business Regulatory Enforcement Fairness Act (SBREFA).

Agriculture. EPA controls the impact of agricultural chemicals, including pesticides and fertilizers, through the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Safe Drinking Water Act, and the Clean Air Act Amendments of 1990. EPA's role is to ensure that the air we breathe and the water available for public consumption are safe and unlikely to cause harm. EPA also takes a secondary role in ensuring that our food supply is safe by enforcing regulations on pesticide application and registration; only certain pesticides may be used on agricultural products destined for the food supply, and only specified amounts may be used.

The risks experienced by farmers and farmworkers are affected by these regulations. Control of the kinds and amounts of pesticides used on agricultural crops reduces the exposure experienced by workers. Further, EPA regulates the *reentry time*, the time workers must wait before returning to a field onto which pesticides were applied. In conjunction with controls placed by other agencies (e.g., OSHA, on work practices), such controls reduce the adverse health impact on the worker. Although worker exposure to pesticides would seem to be squarely within OSHA's purview, a federal court decision in 1974 ruled that EPA's initial reentry rules preempted OSHA. Since then, EPA became the only agency with meaningful enforcement authority for worker exposure to pesticides in many situations.

"Risk Transfer" from the Environment to the Workplace. EPA and OSHA, and a few visionaries in the academic community (see especially Lowell Center for Sustainable Production 2006), have begun to explore the intriguing (and daunting) possibility that compliance with environmental regulations may tend to exacerbate worker exposures. In theory, this problem was recognized decades ago, in special cases such as the attempts to protect ecosystems from lead by encapsulating bridge-repainting projects in large enclosures, which had the side-effect of increasing lead inhalation hazards to the workers within them. In 1999, EPA and OSHA cosponsored a conference (Environmental Protection Agency 1999) to examine whether "risk transfer" was a more general phenomenon, especially as EPA continued to promulgate "maximum available control technology" (MACT) standards for industrial processes under the Clean Air Act. One obvious way to comply with emission limitations from point sources is simply to increase the fraction of a toxic air pollution that remains within the workplace, as apparently has happened in several of the cases detailed in that conference (see, e.g., Piltingsrud et al. 2003).

OVERVIEW OF OCCUPATIONAL RISK ASSESSMENT METHODOLOGY AND POLICY

QRA for environmental exposures, as described in Chapters 2, 3, 4, and 11, shares many of the same fundamental principles with occupational risk assessment. Some of the commonalities and divergences between these two subdisciplines may simply mirror aspects of the risks themselves. Some obvious differences between the two types of risk include the following:

- *Population size*. Whereas many environmental contaminants (e.g., ground-level ozone, fine particulate matter) expose nearly all US citizens to some degree, most of the health hazards OSHA considers affect less than 1% of the national population, and some (see Table 12.6) affect as few as several thousand workers. Therefore, this disparity of a factor of 10^2 to 10^4 in affected

Table 12.6: Lifetime Excess Cancer Risks Associated with All the OSHA Substance-Specific PELs (Set Subsequent to the 1980 *Benzene* Decision)

Substance (Year)	Species Used for Extrapolation	Number of Workers Exposed	Risk at Old PEL	Risk at Average Exposure Level (at Time of Promulgation)	Risk at New PEL
Ethylene Oxide (1984)	Rat	71,000 (directly exposed) 69,000 (indirectly exposed)	(50 ppm) $63–109 \times 10^{-3}$	??	(1 ppm) $1.2–2.3 \times 10^{-3}$
Benzene (1987)	Rat/mouse/human	238,000	(10 ppm) 95×10^{-3}	??	(1 ppm) 10×10^{-3}
4,4′-Methylene-dianiline (1992)	Mouse	4,000	(no prior PEL)	(70 ppb) 6×10^{-3}	(10 ppb) 8×10^{-4}* 9×10^{-4}**
Asbestos (1992)	Human	1,316,000	(2 fibers/cm^3) 64×10^{-3}	??	(0.2 fibers/cm^3) 6.7×10^{-3}
Formaldehyde (1992)	Rat	2,160,000 (at > 0.1 ppm)	(3 ppm) 8.3×10^{-3}** 0.07×10^{-3}*	??	(0.75 ppm) 0.006×10^{-3}* 2.6×10^{-3}**
Cadmium (1992)	Rat/human	525,000	(100 µg/m^3) 58×10^{-3} 157×10^{-3}	??	(5 µg/m^3) $3 \times 10^{-3} – 15 \times 10^{-3}$
1,3-Butadiene (1996)	Mouse	9,700	(1000 ppm) ?? (note: 60 ppm ≈ 99th percentile of exposure)	(1.25 ppm)	(1 ppm) 1.3×10^{-3} to 8.1×10^{-3} (multiple assessments)
Methylene Chloride (1997)	Mouse	240,000	(500 ppm) 126×10^{-3}	(43 ppm) 6.2×10^{-3}** 2.1×10^{-3}*	(25 ppm) 3.6×10^{-3}** 1.2×10^{-3}*
Chromium (VI) (2006)	Human	558,000	(52 µg/m^3) $100–350 \times 10^{-3}$	(2.75 µg/m^3) $\approx 5.5–25 \times 10^{-3}$	(5 µg/m^3) $10 – 45 \times 10^{-3}$
Respirable Crystalline Silica (2016)	Human	2,312,000	(100 µg/m^3 in general industry, GI; 250 µg/m^3 in construction/shipyards, CS) Lung cancer: 11–54 $\times 10^{-3}$ (GI); 33–231 $\times 10^{-3}$ (CS) Silicosis: 85 $\times 10^{-3}$ (GI); 192 $\times 10^{-3}$ (CS)	??	Lung cancer: 5–23 $\times 10^{-3}$ Silicosis: 44×10^{-3}
Beryllium (2017)	Human	61,750	(2 µg/m^3) Beryllium sensitization (BeS): 64×10^{-3} Chronic beryllium disease (CBD): 204×10^{-3} Lung cancer: 140 $\times 10^{-3}$		(0.2 µg/m^3) BeS: 9.3×10^{-3} CBD: 7.2×10^{-3} Lung cancer: 15×10^{-3}

* = maximum likelihood estimate.
** = 95th percentile upper confidence limit.

population size may counteract or exceed the disparity in average concentration, which of course cuts in the opposite direction (occupational exceeding environmental).

- *Population characteristics*. By and large, the general population exposed to environmental hazards is more diverse than the working population. Workers, especially those exposed to chronic health hazards, are generally between ages 18 and 65 and so do not exhibit some special sensitivities to exposures that are peculiar to infants, children, or the very old. Workers are also healthier than many in the general population simply by virtue of being fit enough to perform moderate or strenuous physical labor; hence, epidemiologists are well aware of the "healthy worker effect" that complicates the interpretation of disease rates in occupational cohorts when background rates from the general population are the basis for comparison (McMichael 1976). On the other hand, the fact that workers may have a longer-than-average life expectancy in the absence of additional risk factors does not necessarily mean they are any less susceptible than the general population to these incremental stresses. Although no studies to date have resolved this issue, first principles suggest that many important genetic and other determinants of risk (e.g., variation in enzymes that activate or detoxify carcinogens and other substances) bear no relationship to age or the ability to do work. This observation supports the argument that the occupational population is, on average, no less susceptible than the general population, to say nothing of individuals within either population whose sensitivities may fall anywhere along the spectrum.
- *Exposure patterns*. Occupational exposures are generally confined to 40 of the 168 hours in a week and generally do not extend for much more than 45 years, whereas some environmental exposures approach the theoretical maximum of continuous lifetime exposure, variously assumed to be 70 or 72 years (resulting in an exposure adjustment factor of 45/72). Depending on the mode of action of the substance(s) involved, the intermittent nature of occupational exposures, in addition to extended or other unusual work schedules, can call for a quantitative adjustment (as when bioassay data are adjusted by 5/7 and 8/24 to account for the workweek) or a qualitatively different assessment. Sporadic high exposures can be riskier when compared to continuous lower exposures of a similar TWA exposure that does not exceed a biological threshold; the converse pattern can apply, as when the intermittent exposures allow for physiologic recovery and hence have little chronic adverse effect.
- *Exposure concentrations*. Workplace concentrations of chemical contaminants are often much higher than environmental concentrations. This means that contaminants may cause a range of health effects in workers that are not experienced by the general population exposed to much lower concentrations of the same chemical. For example, workers may be exposed to concentrations that cause acute adverse health effects, whereas the general population may only be exposed to trace levels of the same contaminant. Despite these differences, however, the fact is that most of the agents of particular concern in environmental risk management emerge from workplaces or stem from choices that citizens make both in the workplace and the general environment (e.g., environmental tobacco smoke, which for some people is a fairly constant exposure during the workday and then at home). On the other hand, to the extent that residents and white-collar workers have suffered health effects from exposures to contaminants at and around the World Trade Center site, for example, it was because they essentially experienced occupational levels and patterns of exposure not much different from those encountered by the responders (especially to the extent that some in the latter group, but not the former, had access to respiratory protective devices).

Several persistent differences separate the methods and orientations that environmental and occupational perspectives bring to the *assessment* of the related risks within their own domains. Of note, occupational risk assessment often concerns human exposures within a factor of ten or less of exposures that cause statistically significant increases in adverse health effects in populations of laboratory animals and humans. This is contrasted with a factor of 10,000 or more that is frequently required in environmental assessments. Even more concerning, as an example, the average measured exposure (in the OSHA sampling database) of workers to the neurotoxin and presumed human carcinogen 1-bromopropane was slightly *greater* than the concentration (62.5 ppm) that rodents were exposed to in the National Toxicology Program bioassay of the substance; this concentration caused an 800% increase in tumor incidence in the animals so exposed. The important point here is not only that worker risks are large but also that concerns about the possible errors of overestimation caused by having to extrapolate from "high" to "low" doses simply

don't apply in many occupational situations, where little or no extrapolation is needed. It is not possible that a threshold exists between the (harmful) exposure in a bioassay and the exposure humans face when the latter equals or exceeds the former.

One decision that has impacted how OSHA conducts risk assessment was the Supreme Court's *Benzene* decision (*Industrial Union Department, AFL-CIO v. American Petroleum Institute*; see Vig and Faure 2004). This decision required OSHA to quantify risk rather than merely assert that only the lowest feasible limit was acceptable. OSHA also attempted to update its PELs in its most ambitious health standard of all, the 1989 rule that sought to change over 420 PELs to reflect the current science and to track changes in the TLVs between 1970 and 1989. A federal court struck down all of these limits in 1992 on the grounds that OSHA had not assessed the risk of any of the substances at the old or new PELs (and so OSHA can now enforce only the PELs based on the TLVs as they existed in 1970 plus the relatively few comprehensive standards promulgated since then). OSHA issued four more risk-based health standards in the 1990s and in at least one case pioneered some computational methods and codified evidentiary criteria for replacing a default assumption with a more sophisticated biologic model (see the methylene chloride case study on p. 249).

Court Decisions Affecting Risk Assessment

In two landmark decisions reached less than one year apart, the US Supreme Court concluded first that OSHA must perform QRA and use those results to guide how and how strictly it regulates health hazards. In a separate decision, the Supreme Court clarified that OSHA is not permitted to base its regulations on a quantitative comparison of the monetary value of these risk-reduction benefits to the cost of reducing the risks. Both decisions hinged on the interpretation of Section 6(b)(5) of the Occupational Safety and Health Act of 1970 – that in regulating "toxic materials or harmful physical agents," OSHA must

> Set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life.

In its 1980 *Benzene* decision, the Supreme Court (by a narrow 5–4 vote, with the five justices in the majority issuing four separate opinions explaining their decision) made QRA the cornerstone of OSHA regulation of occupational health hazards and issued the most detailed language to date about the high court's interpretation of several fundamental aspects of risk assessment and management. OSHA issued a final standard governing worker exposure to benzene in April 1977, lowering the PEL from 10 ppm to 1 ppm. At 10 ppm or slightly above, workers exposed to benzene can experience central nervous system effects and diseases of the blood-forming organs (including aplastic anemia, an often-fatal disease); even in the 1970s, there was substantial evidence from human studies that levels of benzene exposure at or below 10 ppm increase the risk of various forms of leukemia. OSHA, however, in line with its Cancer Policy (which it had published in proposed form in 1976), declined to quantify the possible cancer risk either at 10 ppm or 1 ppm; rather, it set the PEL at the lower number on the grounds that while an exposure limit of zero was appropriate for a carcinogen, 1 ppm was the lowest feasible level. OSHA acknowledged that various industrial sectors that use benzene could achieve levels lower than 1 ppm but made a policy judgment that a uniform limit was appropriate. Both the AFL-CIO and the American Petroleum Institute filed petitions seeking to strengthen or weaken the 1977 standard, respectively.

The five justices who voted to invalidate the benzene standard objected on two basic grounds to the central precept of OSHA's Cancer Policy – that carcinogens should be controlled to the lowest feasible level, irrespective of the extent of exposure, the strength of the dose-response relationship, or other factors. First, the Court concluded that Congress did not intend terms such as "a safe and healthful workplace" to mean absolutely risk-free, a condition that literally could only apply if workplaces were shut down. Second, it concluded that a federal agency like OSHA has the responsibility to demonstrate the need for a regulation and cannot shift the burden to the regulated industry to show that the rule is not needed – that in setting the benzene standard, OSHA had "relied squarely upon a special policy [the Cancer Policy] for carcinogens that imposed a burden on industry of proving the existence of a safe level of exposure."

Together, the Court's requirements that OSHA not seek to eliminate all risk (however trivial its magnitude) and that it must marshal evidence to determine a regulation is necessary to "assure that no employee will suffer material impairment of health" add up to a recipe for QRA,

as expressed in the heart of the *Benzene* decision: "[T]he burden [is] on the agency to show that long-term exposure to 10 ppm of benzene presents a *significant risk* of material health impairment" (emphasis added). This conclusion, as the following case studies will demonstrate, immediately changed OSHA from an agency that repudiated QRA to one that had to embrace it as the primary tool for justifying new regulations and for setting the level of stringency.

The *Benzene* decision was much more than a statement that risk must be quantified, however. The Court delved into some of the details about *how* QRA could be undertaken and used, and generally provided OSHA with its blessing to fashion agency risk assessments according to its own policy judgments and scientific interpretations, with the explicit goal of avoiding putting the agency into a "mathematical straitjacket." First, the Court made clear that OSHA could decide for itself what level of risk was large enough to be "significant" and what level was so small it had to be deemed "insignificant." It provided specific (but extremely broad) guidance as to what risks it thought were "plainly acceptable" and which ones were "plainly unacceptable" by stating that an individual risk of one in a billion (10^{-9}) "could not be considered significant," while "a reasonable person might well consider" a risk of one in a thousand (10^{-3}) to be significant. *As Congress has generally instructed EPA (see, e.g., the Clean Air Act Amendments of 1990, and the Safe Drinking Water Act) to regulate risks down to a level of one in a million (10^{-6}), OSHA has thus for the past 40 years been permitted to set standards that match EPA in stringency, but OSHA has rarely if ever come within a factor of 1,000 of this level of protection, often for reasons of technical or economic feasibility of the standard*.

Not only did the *Benzene* decision give OSHA the authority to declare a risk within that broad range "acceptable," but the Court also allowed OSHA to choose a numerical estimate of risk according to its own science-policy judgments and even signaled that it understood that those judgments might be intentionally precautionary:

> So long as they are supported by a body of reputable scientific thought, the agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of over-protection rather than under-protection.

At least in theory, therefore, OSHA could set a PEL for a carcinogen so that the risk to a highly susceptible worker might, even using conservative assumptions, be almost as low as 10^{-9}, so long as it could show that industry could feasibly meet that extremely strict level.

In 1987, OSHA promulgated a revised benzene standard at the same exposure limit (1 ppm) as it had proposed 10 years earlier. In the revised standard, OSHA estimated that the lifetime excess leukemia risk at 10 ppm was approximately 95 per thousand, or 9.5×10^{-3} at the new PEL (OSHA concluded that no lower limit was feasible, even though "significant risk" remained at the newly permissible level). The four justices who dissented from the *Benzene* decision were very concerned that by requiring OSHA "to 'quantify' the risk in order to satisfy a court that it is 'significant,'… [the Court] seems to require [OSHA] to do the impossible." The history of OSHA standard setting over the subsequent 25 years provides ample evidence that using QRA to set risk-based standards is far from impossible. But neither is it easy.

The following year, by a 5–3 vote (one justice did not participate in this case), the Court upheld OSHA's standard limiting the allowable amount of cotton dust in US workplaces (American Textile Manufacturers Institute v. Donovan 1981; see Ashford and Caldart 1996), rejecting the argument of the textile industry that OSHA must weigh the benefit of reductions in health risks against the costs to industry of achieving them. As early as the 1820s, cotton dust was recognized as associated with a progressive obstructive lung disease now known as byssinosis, or brown lung disease. In the United States, roughly 100,000 workers had developed byssinosis by 1970. It should be noted that within a few years of the Court upholding OSHA's regulation, the number of new cases of byssinosis plummeted to less than 25 per year nationwide, although the gradual decline of the US domestic textile industry certainly contributed to this positive development. In 1974, the TLV for cotton dust was lowered to 200 $\mu g/m^3$, and four years later, OSHA promulgated a less stringent set of standards that varied by the industrial process involved, ranging from 200 $\mu g/m^3$ in yarn manufacturing to 750 $\mu g/m^3$ in weaving operations. OSHA performed a thorough QRA of the risk of lung disease from cotton dust at the exposures prevailing at that time and at the proposed new limits and calculated the costs of complying with the standard, but it did not monetize the health benefits and compare them to their costs. The Court said that it "is difficult to imagine what else the agency could do to comply with this Court's decision in [*Benzene*])." OSHA also rejected the petition of the Textile Workers Union of America that the PEL be set at 100 $\mu g/m^3$, on the grounds that the lower limit was not "within the technological capability of the industry."

The Supreme Court emphasized the phrase "to the extent feasible" in the OSH Act, and concluded that Congress did not intend that OSHA engage in cost-benefit analysis, but rather must reduce worker risks "limited only by the extent to which this is capable of being done" – now limited further, of course, by the Court's recent instruction in *Benzene* that OSHA cannot further reduce risks that have become too small to be "significant." Interestingly, the Court described the OSH Act as embracing rather than rejecting cost-benefit thinking, but embracing a brand of cost-benefit balancing that "place[s] the benefit of worker health above all other considerations save those making attainment of this benefit unachievable." In a parallel to *Benzene*, the justices also carved out an interpretation of "significant cost," to clarify when controls that *can* be adopted are nevertheless too expensive to truly be "feasible." They concluded that when OSHA can reasonably show (as it did here) that the industry involved can comply with the regulation and "maintain long-term productivity and competitiveness," it has met its congressional test of feasibility. In fact, the Court explicitly left open the possibility that in the future it might also conclude that OSHA regulation that did threaten the profitability of industry might yet be regarded as "feasible." Therefore, *Benzene* and *Cotton Dust* read together make it clear that OSHA can promulgate health regulations that impose high costs and reduce risks down to small (but not "insignificant") levels.

In practice, over the past decades, OSHA has been prodded, mostly via executive orders enforced by the Office of Information and Regulatory Affairs, to provide all of the detailed information about cost and benefit that an agency that had to compare them quantitatively *would* provide. So whether OSHA ultimately ends up choosing the level of stringency of each standard so as to maximize net benefit, or so as to eliminate significant risk to the extent feasible, these are merely two different ways of considering costs and benefits, and may lead to an identical or similar regulatory decision.

The Mechanics of Occupational Risk Assessment

Occupational risk assessment, as is the case with environmental risk assessment, is generally viewed as consisting of several steps: hazard identification, occupational exposure assessment, exposure-response analysis, and risk characterization, a framework first codified in 1983 (NAS 1983) and still used today. At NIOSH, the institute has developed *NIOSH Practices in Occupational Risk Assessment* (https://www.cdc.gov/niosh/docs/2020-106/default.html), which describes in detail how NIOSH selects the data, conducts QRA, and addresses uncertainty and variability in the resulting risk estimates. The underlying assumptions that NIOSH makes with regard to risk assessment are also described in that document. OSHA generally conducts risk assessment in similar ways as does NIOSH; in promulgating and justifying its regulations, OSHA sometimes makes explicit reference to a NIOSH risk assessment for a given substance, but always also conducts its own independent analysis, which it subjects to rigorous public comment via the public hearings it is required to conduct. The basic steps in occupational risk assessment are described here.

Hazard Identification. As the name would suggest, *hazard identification* is the qualitative association of an activity, location, or pollutant with a hazard. Historically, much of the knowledge that we have on the health effects of certain activities, or that are associated with exposure to environmental contaminants, comes from the occupational setting since in these settings hazards are frequently abundant and exposures are substantial. For example, exposures experienced by uranium mine workers have led to a better understanding of the effect of radiation exposure in the general population. Similarly, repetitive strain injuries were first noticed in manufacturing settings, where repeated motion is common. Later, it was noticed in office workers and in the general community. However, it is unlikely that study of nonoccupationally exposed individuals alone would have led to the insight obtained from those exposed in workplace settings. Exposures are generally greater, and for a longer duration, making the hazard more readily identifiable in the occupation exposed.

Hazard identification alone does not indicate anything quantitative about the risks of chemical exposure. In the case of carcinogens, several agencies and organizations classify chemicals with regard to their carcinogenicity without necessarily conducting a quantitative analysis (exposure-response analysis) to estimate risks. The National Toxicology Program, the EPA, and the International Agency for Cancer Research routinely assess the evidence for carcinogenicity and make a hazard determination for chemicals of interest (and sometimes for industrial processes and even occupations). These organizations classify carcinogens as "known to cause cancer in humans" or "reasonably anticipated to" (EPA further divides the category below "known" into "probable" and "possible" carcinogens. NIOSH uses the information from these three organizations to make a determination whether a chemical is an occupational carcinogen, and OSHA

requires manufacturers to report on their Safety Data Sheets the results of NTP, EPA, or IARC hazard identification determinations. In making its assessment, in addition to the carcinogen classifications, NIOSH takes into consideration the occupational relevance of the evidence supporting carcinogenicity (NIOSH 2016a).

Occupational Exposure Assessment. Industrial hygiene (also called occupational hygiene) focuses on the exposures experienced by individuals who work in industrial or occupational settings and may be viewed as a branch of the larger science of exposure assessment. Some definitions are needed to start. These include the *concentration* of pollutants in an environmental medium, the *exposure* experienced by an individual, and the *dose* received by the individual.

1. *Concentration, exposure, and dose differentiated.* An important distinction to be made is between the related concepts of concentration, exposure, and dose. Consider the following scenario: A worker is required to enter an enclosed space that formerly was filled with a volatile solvent. The atmosphere in the enclosed space is saturated with the vapor of the solvent.

   In order to assess the experience of the worker, we must consider three different concepts: concentration, exposure, and dose. The concentration in the tank (i.e., space) is relatively simple to understand: it is the saturation vapor pressure of the organic solvent. It can be readily measured using appropriate instrumentation or estimated from the physical and chemical properties of the solvent. This is the concentration that the worker experiences in the enclosed space. But what is her exposure? Exposure, defined as the amount of hazardous substance delivered to some body boundary, can come from one of three different *routes*: inhalation, for which the lung epithelium is the boundary of interest; ingestion, for which the gut epithelium is the boundary of interest; and body-surface contact, for which a body surface, usually the skin, is the boundary of interest. Dose, on the other hand, is the quantity of chemical that crosses the boundary and enters the body. Estimation of dose frequently depends on the mode of toxicity. If a chemical is direct-acting at the exposure interface, dose and exposure would be identical. However, if a chemical must be absorbed through the lung, gut, or skin, and then metabolized to an active agent before being distributed to the organ of interest, the dose (sometimes called effective dose or toxic dose) may be quite different from the exposure. For example, if the chemical must be absorbed through the lung into the blood stream, distributed to the liver, where it is metabolized and then the active metabolite distributed to the brain to produce the health effect, the actual effective dose would be very different from the exposure. For most chemicals, we don't know enough about the critical steps in absorption, metabolism, distribution, and elimination of the chemical to precisely determine the effective dose, so, in many cases, exposure and dose are used interchangeably in the scientific literature.

2. *Pathways.* The specific ways the pollutant moves through the environment can be many and varied and should be distinguished from *routes* of exposure. Here is a simple example to distinguish these two concepts better. One may be exposed to sulfur dioxide in various ways, the majority of which lead to exposure through the inhalation route. One particular pathway is the generation of sulfur dioxide through the combustion of sulfur-containing coal, followed by the concomitant release of this gas from the combustion facility, and advection and dispersion in the air. An alternative pathway in an industrial setting might arrive from the use of sulfurous acid in a manufacturing process with the concomitant release of sulfur dioxide at an individual workstation. The worker at his workstation is then exposed directly to sulfur dioxide via the inhalation route. These two pathways differ substantially and would require entirely different control strategies to reduce exposure. However, since both exposures are through the inhalation route, the risk assessment process would be similar. At this point, the determination of exposure requires us to gather much more information about the scenario. In the exposure scenario where a worker is entering a tank with saturated vapor, the worker should be provided with a respirator that supplies air from outside the tank, as it would be much too dangerous to send an individual into such an enclosed space without such a device. For a saturated vapor in an enclosed tank, the primary concern would be inhalation exposure. If the respirator was fitted perfectly and functioning properly, the worker's inhalation exposure would be close to zero. However, respirators may be used improperly or not at all, resulting in inhalation exposure greater than expected under this ideal scenario. However, the worker would also receive exposure through the skin; thus dermal exposure may be an important route and potentially could result in health effects. We must be careful to consider all potential routes and attempt to identify all pathways of exposure.

3. *Magnitude, frequency, and exposure duration*. It is also important in understanding exposure to look at the time course of the exposure, sometimes referred to as the *exposure profile*. The definition of exposure requires averaging over time that, in turn, results in a great deal of lost information. Intuitively, we may imagine that exposure to a very high concentration of contaminant for a short duration followed by exposure to no concentration at all for the remainder of, say, a work shift may have different consequences from exposure to a modest concentration over the entire work shift. The total would be the same, but the duration and concentration of exposure would be different. For example, one worker may be welding for 15 minutes in a relatively enclosed space and be subjected to a concentration of metal fumes of 40 mg/m^3. He thus receives an exposure of 40 $mg/m^3 \times 0.25$ h = 10 $mg/m^3 \times 1.0$h. After welding, he goes on to different activities in a different part of the facility in which he experiences no concentration of welding fumes and thus receives no further exposure during the shift. His coworker, working in the same area but not exposed directly to the fumes, remains for the entire eight-hour shift. Measurement of metal fume concentrations over the course of the day in the location of the second worker gives 1.25 mg/m^3. The worker in this location receives an identical exposure: 1.25 $mg/m^3 \times 8$ h = 10 $mg/m^3 \times 1.0$ h, but the pattern is different. Depending on the chemical exposure, the health consequences may also be different. To account for such differences, it is important for the exposure assessor to be cognizant of the magnitude, frequency, and duration of the exposure. One should always ask, what is the peak concentration experienced during the monitoring period? Does it differ significantly from the mean concentration? How frequently are high-concentration peaks found? Are the concentrations relatively stable, or is there a good deal of variability from minute to minute or hour to hour? Do the peaks recur regularly or episodically? What is the duration of the exposure? Is it short followed by no exposure, or does it occur at moderate levels for a long period? Such information can prove invaluable in both assessing the risks of chemical exposure and in addressing potential effects and control strategies.

4. *Methods of exposure assessment*. Exposure assessors typically undertake exposure assessment investigations in one of two ways: (1) direct exposure assessment methods and (2) indirect exposure assessment methods. Direct exposure assessment methods involve outfitting an individual with some type of monitor that measures pollutant concentrations experienced by the individual as he goes about his daily activities. This is most easily visualized for airborne contaminants. In this case, an air monitor collects a sample of the air breathed by the individual over a period of time. That air sample is then analyzed for the contaminant of interest either on a real-time or time-integrated basis (both are commonly used in occupational settings). Similar monitors may be envisioned for exposures occurring via the ingestion or dermal pathways as well. By the direct method, actual exposures experienced by an individual can be observed. This is a major strength in assessing exposure and is generally desirable. However, portable monitors may not exist for the particular contaminant under investigation, or may unduly influence the activity patterns of the individual; that is to say, the normal activities that are undertaken in the workplace. They also may be bulky, require an electrical connection, or otherwise interfere with job duties.

   An alternative strategy involves indirect exposure assessment, in which microenvironments, or areas, or activities likely to give similar and relatively homogeneous exposures are monitored using, perhaps, more sophisticated monitoring equipment and where the movement of the individual within and between such microenvironments is noted. Again, the inhalation route is most easily visualized. In this case, air pollution monitors are placed in various locations (e.g., workstations) to determine concentrations found in these locations. Exposure is then determined by having the individual note the amount of time spent in each of the microenvironments, multiplying the concentration measured by the amount of time spent in the microenvironment, and adding all such values together. For other routes of exposure, a similar approach can be used.

   Yet another strategy, one not involving any direct measurement, can also be envisioned. With this strategy, an activity pattern for an individual can be assumed, perhaps through a large data-gathering effort addressing the locations where individuals typically spend their time. An example is the job-exposure matrix in which certain job titles are assumed to have homogenous and known exposures. Such an approach is used often in occupational epidemiology. An example might include distinguishing between two groups of workers (e.g., manufacturing-line workers and office workers) at the same location. Office workers might be assumed to have low

(or even no) exposure, while manufacturing-line workers receive high (or perhaps even quantified) exposures.

5. *Biological markers of exposure*. Exposure to environmental contaminants requires the simultaneous presence of a contaminant concentration and a human subject to receive the exposure. Both the direct and indirect methods described previously assume that the exposure occurs if these two components exist. However, the only way to be sure is to use the response of the human subject as a measure. This is what exposure assessors do when they use biological markers (sometimes referred to as *biomarkers*) of exposure. Biological markers of exposure to a given contaminant make use of biological material (e.g., exhaled breath, urine, blood or blood components, fecal samples, or tissues). These samples are analyzed for the contaminant in question, called the *parent compound*, or a metabolite or biological by-product to determine the exposure. Occupational exposure to trichloroethylene, an important industrial solvent, offers a good example. Urine samples can be taken from individuals and analyzed both for trichloroethylene and for its metabolites (e.g., trichloroacetic acid) to ascertain exposure to this class of compound. Using measures of these two compounds, we can infer the magnitude of the initial exposure and, through analysis of the metabolic processes involved, the timing of such exposure.
6. *Other exposure-related issues*. Unlike the technology-based standards that the EPA sometimes sets, which require the estimation of exposures once the required controls are installed, OSHA PELs fix the maximum post-regulatory concentration. In other words, there is no need to estimate future exposures, as the regulation itself determines what is allowable. OSHA standards are compared to the actual exposures of individuals, rather than the environments they live or work in; an employer is deemed to be out of compliance if a personal air sampling device attached to a worker shows a concentration above (with statistical significance) a PEL.

Occupational PELs assume that a worker is employed over a 45-year *working lifetime* (essentially from age 20 through age 65) and that risk is accumulated during this period. Contrast this to the full 70-year lifetime assumed by the EPA when projecting cancer risk. Some have suggested that since individual industries and worksites are regulated, exposure – and thus risk – should only be accumulated during the time that the average worker remains with a single employer, perhaps 10 to 15 years (see, e.g., Burmaster 2000). This argument is weak in that workers normally change jobs within the same industry and are likely to continue accumulating exposure during their next job as well, if not to the identical substances then to similar ones that act via a common toxicologic mechanism. Workers should be protected for their entire working lifetimes.

OSHA is required to perform exposure assessment when promulgating a regulation. It must, for example, account for the exposures experienced prior to the regulation being put in place and for likely compliance discrepancies. That may result in an over- or underexposure experienced by the workers themselves. This is especially noteworthy because, in practice, working facilities are normally considered to be in compliance if measured concentrations of contaminants at the site are less than 125% of the PEL. Further, compliance requirements allow conversion of exposure measurements that take place over less-than-full to full-shift exposures assuming zero exposure during the remaining shift time, biasing inferred exposures. In addition, no allowance is made for previous exposures; exposures are assumed to be fresh each day with no accumulated effects.

Dose-Response Analysis

In occupational risk assessment, dose-response analysis can be used with epidemiological data or animal bioassay data to predict health impacts on workers. Data collected as part of an occupational epidemiology study are generally regarded as the ideal data for dose-response (also called exposure-response) analysis because there is by definition no need to analogize across species to estimate human risk. Ideally, if sufficient exposure data have been collected or estimated, measurements can be linked to individual work histories and health (or death) records to permit dose-response estimation for the working population. Occupational epidemiological studies, however, are typically conducted for only a small fraction of a working lifetime, so even when these data are available, assumptions must be made to estimate health effects from exposure over a working lifetime. This requires understanding the disease process, the mode of action of the chemical exposures, and sophisticated statistical modeling of the available data. One example of an occupational epidemiologically-based risk assessment is the NIOSH risk assessment for diacetyl (a chemical found in butter flavoring). In that assessment, NIOSH modeled the change in lung function

in workers exposed to diacetyl in popcorn manufacturing. Statistical modeling of the exposure data collected and measurements of lung function led to NIOSH recommendations for a REL for diacetyl (NIOSH 2016). For more information on how to use epidemiological data in occupational risk assessment, see *NIOSH Practices in Occupational Risk Assessment* (NIOSH 2020).

In contrast, animal bioassays require interspecies extrapolation for human risk assessment, but they do allow assessors to consider carefully controlled exposures rather than concentrations workers happen to have already encountered. In animal studies, generally, a relatively small number of animals are exposed to the compound of interest at several levels, up to (and often including) a significant fraction of the *maximum tolerated dose (MTD)*. The MTD is defined as the highest dose of the test agent during the chronic study that can be predicted not to alter the animals' longevity from effects other than carcinogenicity. In many cases, cancer is the outcome of interest, and tumor development in the animal is the way such an outcome is quantified. The number of dose groups in such an investigation is quite limited, often consisting of no more than three or four; these may include a control group receiving no exposure, an MTD/2 group that receives a high dose, and another group (or two) at lesser fractions of the MTD. In general, but not always (see 1-bromopropane example on p. 252), these doses are higher than might be experienced in a normal, nonoccupational setting, even under the most adverse conditions.

A significant question then becomes, how do we extrapolate the effect seen at the high levels of exposure experienced by the animals to the low levels experienced by the human subjects facing the exposure in an environmental or occupational setting? This is not as simple as it seems; there are many ways to do the low-dose extrapolation, and unfortunately, they often give significantly different answers. One common procedure for estimating the effect of low concentrations is the mathematical modeling of the dose-response curve. When the exposure of interest is to a genotoxic carcinogen, a model known as the *linearized multistage model* (LMS) is often used. The models typically use the data for all of the dose groups to estimate the probability that an animal receiving a given dose would develop cancer. This approach may be used alone or in combination with the benchmark dose (BMD) approach, in which the dose response is modeled down to a pre-defined point of departure and then a linear extrapolation is applied to estimate the risk levels of interest. We will not discuss the details of the LMS or BMD analysis here, but we will point out that in both these approaches, there is an implicit assumption in the model that at low doses, the probability of an adverse health outcome increases with increasing doses (in other words, that there is no threshold).

Once the data are fit using the LMS or BMD, we must account for differences between human beings and the rodents who are exposed in order to determine an occupational exposure limit. Typically, to account for the differences in size between, say, mice and human beings, risk assessors scale the dose by a function of the body-weight (BW) ratio. $BW^{3/4}$ is typically used as metabolic processes scale approximately this way. Risk assessors often also typically look at the quality of the statistical fit to the dose-group data and use the *upper confidence limit* (UCL) on the linear slope value. That is, the statistical fit would give a number, called the *maximum likelihood estimate* (MLE), but to account for some uncertainty in the slope estimation, risk assessors frequently assume a larger slope based on the variability in the observed response. This assumption is slightly "conservative," but the UCL cannot be more than a factor of about 4 above the expected value of the slope (as can be seen in Hattis and Goble 1991).

Not all occupational risk assessments have followed this approach. For some occupational standards, BW extrapolation has been done in a linear fashion; that is, the scaling is BW^{1}. This is less protective, by roughly a factor of 4 (when rat data are used) or 7 (mouse data) than $BW^{3/4}$. Further, the MLE estimate is sometimes taken, rather than the UCL on the plausible slope of the dose-response function, again affording less protection.

For chemicals that have health effects other than cancer (for example, liver toxicity, neurological effects, or respiratory irritation), the dose-response analysis typically includes the assumption that there is a threshold below which the body either does not experience toxicity or can recover from that toxicity. Modeling animal toxicity data for those types of health effects has some similarities and some differences from modeling carcinogenicity data. Extrapolation of animal data to humans is often done similarly to cancer data. But, since a threshold of toxicity is assumed, the modeling may be a bit different. In the case of noncancer health endpoints, typically the statistical model that may best fit the data is unknown, so a BMD approach, in which several models are fit to the data, is used. Once the results are obtained, the model fits are compared and a best-fitting model is selected. This can be done by inspection of the model fits or by using a statistical procedure called Bayesian model averaging in which the statistical weight of each model is estimated based on how

well the model fits the data. The result of this is a statistically weighted "average" model that represents an amalgam of the models used in the analysis based on their individual model fits. Often this provides a superior model fit to selecting a "best-fitting" model by inspection.

Once a best-fitting model is established, the BMD is estimated at a prescribed benchmark response (often 10% for incidence data). Adjustment factors (sometimes called uncertainty factors) are then applied to the benchmark dose to estimate a dose below the BMD that may also fall below the presumed biological threshold of toxicity. These factors account for interspecies variability in metabolism and susceptibility, interindividual variability in metabolism and susceptibility, differences in the experimental duration and the desired exposure duration (e.g., working lifetime), sufficiency of database, and other considerations. Rather than estimating a prescribed risk level (for example, 1 excess case of cancer per 10,000 workers exposed for a working lifetime), the final exposure value for noncancer health effects is one presumed to be unlikely to produce irreversible harm in more than a small portion of the more susceptible subpopulation – colloquially, a "safe" level.

Case Study: Methylene Chloride

OSHA's 1997 regulation imposing various restrictions on the industrial use of methylene chloride (MC) provides an unusually wide-ranging look at the scientific and science-policy issues that can arise in writing and implementing a risk-based regulation. QRA featured prominently in several of these issues and provided OSHA with an opportunity to innovate in ways that made the MC regulation a cutting-edge one for its time. MC is a very common chlorinated solvent (US production in 2016 was approximately 270 million pounds), with uses ranging from stripping paint to industrial degreasing to gluing together pieces of polyurethane foam (as in the manufacture of upholstered furniture). The paint-stripping process often involves immersing the object in a tank of liquid MC, as when stripping furniture, or by spraying an MC solution onto large objects, as when repainting airplanes. All of these processes give ample opportunity for occupational exposure. OSHA began considering a regulation for MC in the late 1980s when the United Auto Workers and other unions petitioned OSHA to that effect (during the same period, the FDA banned the use of MC in aerosol cosmetic products). At the time, OSHA estimated that approximately 250,000 US workers, employed at roughly 90,000 different establishments (many of them obviously very small businesses), were exposed to MC. Although OSHA adopted a PEL of 500 ppm for MC when the agency was created in 1970, its surveys suggested that almost all of those workers were exposed to concentrations lower than 500 ppm – but that an estimated 60,000 workers routinely encountered concentrations between 25 ppm and 200 ppm.

MC can cause a variety of adverse health effects in experimental animals and in humans. At roughly 2,000 ppm, MC can cause death by asphyxiation; between 1980 and 2018, one group of researchers (Hoang et al. 2021) found reports of 85 fatalities from accidental overexposures to MC, generally in confined spaces such as tank trucks, but also in larger enclosures as in the use of MC to strip paint from the floors of poorly ventilated rooms. In concentrations at or below the 500 ppm PEL, MC can cause central nervous system depression in humans and (because MC is metabolized to carbon monoxide) can increase blood carboxyhemoglobin concentration, raising concern about potential acute and chronic cardiovascular effects. The critical effect in the development of the PEL for MC, however, was its potential carcinogenicity: a well-conducted National Toxicology Program bioassay in male and female mice showed significant excesses of malignant lung and liver tumors in animals exposed by inhalation to roughly 2,000 ppm MC, only a factor of four above the prevailing PEL. Epidemiologic studies of workers exposed to MC did not provide clear evidence of carcinogenicity, although most of the studies involved relatively small populations in relatively well-controlled operations. For example, one prominent study examined 1,300 workers whose average MC exposure was only 26 ppm, a level that OSHA eventually concluded would have yielded an excess cancer risk of roughly 3 cases per thousand, essentially statistically indistinguishable in a cohort of this size, given the much higher natural background rate of lung and other cancers in the normal population.

In light of this evidence, OSHA ultimately promulgated regulations setting a PEL of 25 ppm and a STEL of 125 ppm (so that no exposure averaged over 15 minutes shall exceed the STEL). OSHA estimated that the excess lifetime cancer risk at the new PEL was approximately 3.6 per thousand, substantially higher than the 10^{-3} benchmark referenced by the Supreme Court in 1980 as clearly significant risk. OSHA determined, however, that 25 ppm was the lowest level that all affected industry sectors could feasibly meet (although in no case did OSHA estimate that the cost

of complying with the standard would amount to more than 2% of the sales revenue of affected firms). Neither the labor unions nor the affected industries challenged the standard in court after OSHA agreed to make minor changes in one ancillary provision of the standard and to allow several additional months for certain industry sectors to come into compliance. OSHA also estimated, considering the number of workers then exposed to various concentrations of MC, that the new standard would prevent approximately 30 cancer deaths per year and would cost US industry roughly $100 million per year (over a ten-year period) to implement.

Although the general provisions in the MC standard deviated little from the template OSHA had used for its other substance-specific standards after the *Benzene* decision, OSHA's risk assessment for MC broke new ground in at least three major respects.

1. *Incorporation of a metabolic model for interspecies extrapolation*. By the early 1990s, MC had become perhaps the single most extensively studied industrial chemical with respect to the pathways and rates governing its metabolism in both rodents and humans. Various research groups had reached a consensus that both rodents and humans metabolize MC via two competing biochemical pathways: a mixed-function oxidase system that converts MC to carbon monoxide and a pathway involving the enzyme glutathione-S-transferase (GST), which produces at least two reactive intermediates known to interact with DNA and RNA. This information allowed the development of physiologically based pharmacokinetic (PBPK) models of the metabolism of MC in rodents and humans. PBPK modeling is a method for estimating the exposure to a metabolite of a chemical when there are data available on the absorption, distribution, metabolism, and excretion of the chemical in the body, *and* the metabolite that causes the toxicity of interest has been identified. An understanding of both the disposition of the chemical in the body and its toxic mode of action is necessary for PBPK modeling to be useful in risk assessment. In the case of MC, the data were available to support PBPK modeling.

   PBPK modeling offered an opportunity for OSHA to estimate risk in light of both the uncertainty in interspecies extrapolation (from mice to humans) and the variability in how different humans metabolize MC. With the help of scientists from two universities and a state health department, OSHA refined the basic PBPK model published in the scientific literature, incorporating quantitative measures of uncertainty in the 46 different parameters (23 in mice and a corresponding number in humans) needed to run the model, as well as measures of pairwise correlation between all relevant parameters. The thought process that led OSHA to conclude that the PBPK approach to assessing MC risk was superior to the default assumption also enabled OSHA to implement one of the major recommendations of both the 1983 and 1994 National Academy of Sciences risk assessment committees that agencies describe for the interested public the quantity and quality of information they deem necessary to depart from a generic default so that researchers can investigate specific questions productively and other stakeholders can gauge whether the agency followed its own advice in making such crucial science-policy decisions. As a result of this experience, OSHA developed a list of 11 scientific criteria to evaluate using these types of data in future chemical risk assessments (Exhibit 12.1) This decision represented the first time a US federal agency set a regulatory occupational exposure limit for a toxic substance using a PBPK model for interspecies extrapolation rather than an extrapolation method, such as a BW or surface-area ratio (see Kuempel et al. 2015 for a discussion of the 11 OSHA criteria in context of improving occupational risk assessment).

2. *Rejection of an alternative theory claiming that MC causes cancer in mice but not in humans*. As part of the rulemaking effort, OSHA also evaluated a series of journal articles, which postulated that humans are insensitive to the carcinogenic effects of MC seen in mice. A petition that OSHA reopen the hearing record to evaluate these articles claimed that

   This research, which is now complete, shows that mice … are uniquely sensitive at high exposure levels to MC-induced lung and liver cancer, and that … there are no foreseeable conditions of human exposure in which the carcinogenic effect seen in mice would be expected to occur in man.

   This assertion was based on several hypotheses, including (1) that MC produces lung tumors in a type of cell (the Clara cell) that may be relatively more abundant in mice than in humans, (2) that mouse liver and lung cells may be more susceptible than human cells to single-strand DNA breaks when exposed to MC, and (3) that the GST enzyme that metabolizes MC may be more abundant in mouse cells than in human cells and that it can be found in the nuclei of mouse cells but may tend to concentrate in the cytoplasm of human cells (i.e., not in as close

EXHIBIT 12.1 OSHA'S SCIENTIFIC CRITERIA FOR ACCEPTING A PBPK MODEL

1. The predominant and all relevant minor metabolic pathways must be well described in several species, including humans. (Two metabolic pathways are responsible for the metabolism of MC in humans, mice, rats, and hamsters.)
2. The metabolism must be adequately modeled. (Only two pathways are responsible for the metabolism of MC as compared to several potential routes of metabolism for other compounds, such as benzene and dioxins. This simplified the resulting PBPK models.)
3. There must be strong empirical support for the putative mechanism of carcinogenesis (e.g., genotoxicity), and the proposed mechanism must be plausible.
4. The kinetics for the putative carcinogenic metabolic pathway must have been measured in test animals in vivo and in vitro and in corresponding human tissues (lung and liver) at least in vitro, although in vivo human data would be the most definitive.
5. The putative carcinogenic metabolic pathway must contain metabolites that are plausible proximate carcinogens (e.g., reactive compounds such as formaldehyde or S-chloromethyl glutathione).
6. The contribution to carcinogenesis via other pathways must be adequately modeled or ruled out as a factor. For example, there must be a reasonable analysis of why reactive metabolites formed in a second pathway would not contribute to carcinogenesis (e.g., formyl chloride produced via the mixed-function oxidase (MFO) pathway is likely to be too short-lived to be important in MC carcinogenesis).
7. The dose surrogate in target tissues (lung and liver in the case of MC) used in PBPK modeling must correlate with tumor responses experienced by test animals (mice, rats, and hamsters).
8. All biochemical parameters specific to the compound, such as blood:air partition coefficients, must have been experimentally and reproducibly measured. This must be true especially for those parameters to which the PBPK model is most sensitive.
9. The model must adequately describe experimentally measured physiological and biochemical phenomena.
10. The PBPK models must have been validated with data (including human data) that were not used to construct the models.
11. There must be sufficient data, especially data from a broadly representative sample of humans, to assess uncertainty and variability in the PBPK modeling.

Source: Occupational Safety and Health Administration (1997, pp. 1533–1534).

proximity to the cell's genetic material). OSHA invited the scientific community and other interested parties to review the published studies on this topic. Various experts commented that mice and humans can differ *quantitatively* in their sensitivity to MC and that the PBPK approach accounted for such quantitative distinctions. Commenters also disputed the notion that mouse and human GST could only exist in fundamentally different portions of the cells of each species. By evaluating new and emerging science and by engaging experts in the process, OSHA demonstrated that this approach can significantly improve the quality of risk assessment.

3. *Estimating individual risk for a hypothetical person of above-average susceptibility to exposure-related disease*. When OSHA calculated the excess cancer risk of exposure to 25 ppm MC using the PBPK model, it arrived at a slightly lower average value of risk than it had predicted using a simple BW extrapolation several years previously (1.2×10^{-3} versus 2.3×10^{-3}). However, all of the information on uncertainty and interindividual variability needed to calibrate and run the PBPK model allowed OSHA to explore what the excess risk would be to workers with differing degrees of susceptibility to MC (at least those differences due to variation in individual metabolism) and with different assumptions about uncertainty.

Ultimately, OSHA determined that it would be more responsive to the spirit of the OSH Act language that "no employee shall suffer material impairment of health" if it estimated risk for a

worker of above-average susceptibility. Due to either uncertainty or interindividual variability (or a combination of both), OSHA estimated there was approximately a 5% chance that the excess risk to a randomly selected worker would be at least threefold higher than the mean value of 1.2×10^{-3}, and so it based its final PEL on the basis of this 95th percentile estimate of 3.6×10^{-3}. To our knowledge, this was the first time that a US federal agency quantitatively analyzed interindividual variability in susceptibility to a toxic substance and explicitly estimated risk to consider persons of above-average susceptibility. Note that the PEL of 25 ppm did not meet the *Benzene* decision criterion that risk be reduced at least to 10^{-3} because OSHA determined that a lower level would not be economically feasible for all affected industry sectors.

In June 2020, EPA finalized its comprehensive risk evaluation of MC and found unreasonable risks to consumers from all consumer uses of MC and to workers from most commercial uses of MC. Additionally, EPA found unreasonable risks from most commercial uses of this chemical to workers nearby but not in direct contact with MC (which EPA refers to as "occupational non-users"). These determinations were based on consideration of both short- and long-term inhalation and dermal exposure. In response to determinations of unreasonable risks to workers and consumers, EPA banned sales of MC in paint and coating removers for consumer use and, as of this writing, is considering additional risk mitigation strategies for workers.

Frequently, when chemical regulations are promulgated, companies move to substitute different, less regulated, often less well-studied chemicals. This is called a risk-risk trade-off (Graham and Wiener 1995; Sunstein 1996). One example of this is the substitution of 1-bromopropane (synonym: *n*-propyl bromide), as an alternative to MC. At the time that the OSHA MC regulation was taking effect, both this compound and a more toxic contaminant (2-bromopropane) formed during its synthesis were known to cause both neurological and reproductive damage in laboratory animals, and the National Toxicology Program concluded in 2003 that at current occupational exposure levels, 1-bromopropane poses "serious concern for reproductive and developmental effects in humans" (NTP 2003). In addition, in 2004, Robinson reported (Robinson 2004) that six workers in a foam cushion factory in Utah developed chronic neuropathic pain and difficulty walking after being exposed to approximately 130 ppm 1-bromopropane over a period of several months (see also Urbina 2013). The National Toxicology Program conducted inhalation bioassays on 1-bromopropane and found there was clear evidence of carcinogenic activity of 1-bromopropane in female rats and female mice and some evidence of carcinogenicity of 1-bromopropane in male rats.

BOX 12.4 MORE RISK-RISK TRADE-OFFS IN OCCUPATIONAL HEALTH AND SAFETY

Adam M. Finkel

Although some trade-offs do seem inevitable (for example, that the benefits of reducing ground-level ozone will be offset to some extent by the additional skin cancers that will result from lower ozone concentration), questions remain about whether in general claims of dire secondary outcomes from reducing existing risks are wholly legitimate. Among other claims, various industries warned OSHA (and the Office of Information and Regulatory Affairs) during the final stages of OSHA's methylene chloride rulemaking that the MC standard would result in a rash of fires and explosions as companies that could not meet the standard were forced to switch to acetone – a flammable substitute – as a solvent, adhesive, and so on. Similarly, the trade association representing operators of general aviation aircraft warned that "without MC," repainting of these aircraft would have to be done using substitute paint strippers, which could lead to substandard or less frequent paint removal and "a major risk factor to the flying public" from corrosion and metal fatigue under the paint going undiscovered (House Subcommittee on Workforce Protections 2001). At the time, OSHA told both Office of Management and Budget (OMB) and the congressional oversight panel that it did not anticipate widespread substitution away from MC (that the new exposure limit could easily be met in these and other sectors) and that in any event, these industries were capable of handling substitutes safely and producing safe products. Now that ample time has elapsed in which any dire offsetting risks would have been evident, it appears that there has been at most one significant industrial fire or explosion involving acetone in processes where MC might possibly have been used (to be sure, that number was near zero prior to the issuance of the MC standard as well), and no reported general aviation accidents where improper paint stripping was a factor.

Although OSHA still does not have a PEL for 1-bromopropane, ACGIH set its TLV at 0.1 ppm in 2016, and in 2021, EPA made 1-bromopropane the first "new" addition to its list of 188 Hazardous Air Pollutants since the Clean Air Act Amendments became law in 1990 (based on petitions filed in 2010 and 2011 by a state environmental agency and an industry trade association).

CONTROL OF HAZARDS

In an effort to manage risk to the worker, several types of control strategies are recommended. Employers should follow the hierarchy of controls that OSHA, NIOSH, and EPA emphasize in their communication, pursuing each strategy from first to last before moving to the next one: elimination, substitution, implementation of engineering controls, administrative controls, and the use of personal protective equipment. This hierarchy is designed to encourage employers to make process changes that remove the risk entirely or, failing that, to reduce exposures through engineering controls and – only if these are not feasible – to resort to measures that place extra burden on workers themselves. Let us examine each of these controls (Figure 12.3).

Elimination

The first option for removal of hazards in the workplace is the elimination of the hazardous substance or process entirely. This, of course, eliminates the hazard once and for all and offers complete protection for the worker. Unfortunately, this is not always possible. Some activities, such as the operation of hazardous machinery, cannot be removed from the workplace. Some consumer products could be discontinued entirely, but this is often fraught given our market economy. Hence, alternative control strategies must be invoked.

Substitution

If a material, a process, or an individual piece of equipment is by its very nature hazardous, a reduction in risk for the worker may be efficiently achieved through the substitution of a less-hazardous process, equipment, or material. Workers would then no longer be exposed to the original hazard, but rather to a different and lesser one. This is an effective strategy and may offer long-run cost reduction in that lost worker time is reduced along with reduced workers' compensation costs. Initial capital outlays may be large, however, especially if a process must be revamped

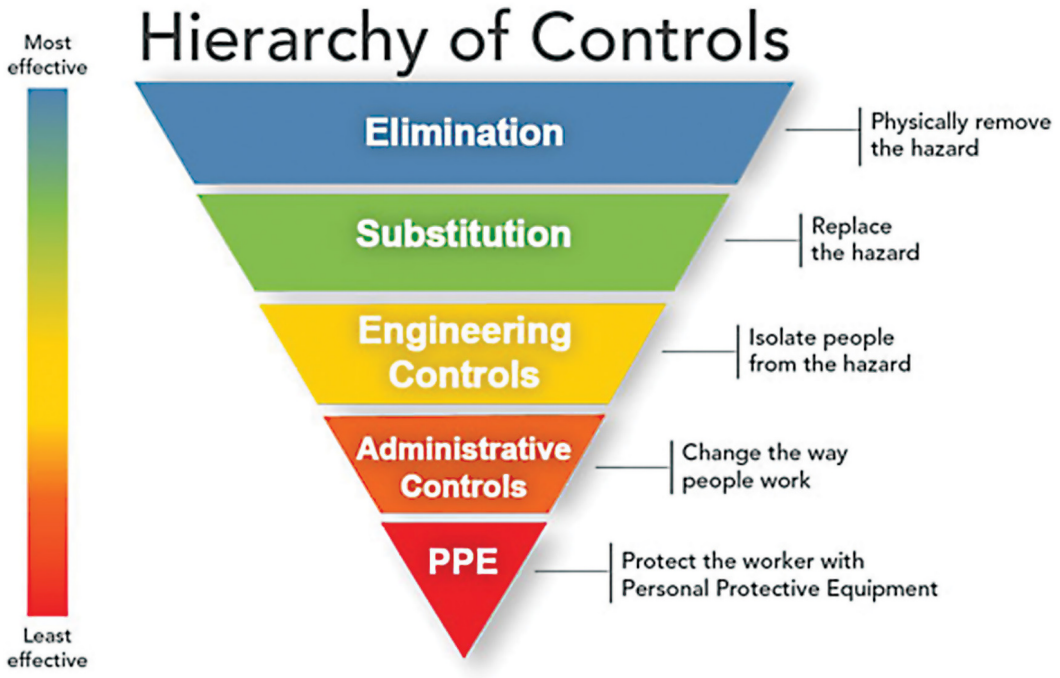

Figure 12.3 The NIOSH Hierarchy of Controls.

entirely. Development of an effective substitution strategy requires a good deal of thought as well as experience in developing the new procedures.

Process Substitution. The substitution option may be most clearly indicated using some examples. In automotive manufacturing, for example, painting may be accomplished using a spray bay in which aerosolized paint is applied to the metallic frame of the automobile. The potential for inhalation exposure is great in such a spray, and the hazard associated with inhalation of paint and solvent vapors is well understood. An effective substitute for this process, whereby the metallic frame of the vehicle is dipped into the paint, thereby reducing aerosolization and exposure, is readily envisioned and has been implemented. The implementation of such a substitution is not without difficulties, however. New paint formulations must be developed that afford good adhesion and attractive finished products. Even drying is problematic and requires a further change in the process. A significant retooling of the painting component of an assembly line for automaking is the indirect result of this hazard reduction.

Equipment Substitution. While modification of a process offers the best reduction in risk for the worker, the cost of such a modification may be prohibitive. The change of a single piece of equipment may be sufficient to reduce risk substantially at a much lower cost. The selection of replacement equipment often requires the expertise of both management and worker in that the financial investment will be supplied by the management side, while familiarity with the process and working environment will be better known to the worker.

Consider the case of solvent use in an occupational setting. Small quantities of solvents are often delivered in glass bottles ranging in size from 250 mL to 4 L or more. The larger bottles are relatively difficult to handle and may be dropped or dislodged from their storage area with the potential for significant exposure to the worker. Replacement of such bottles by safety storage cans that are unbreakable, or by enclosing the bottle in a plastic case, substantially reduces the risk of breakage. Such modification of storage equipment can be done at low cost and often offers a significant improvement in worker safety.

Material Substitution. In an industrial process, it is often necessary to use hazardous materials. However, the substitution of a less-hazardous material for a more hazardous one can often be affected without loss of efficiency in the process overall. Consider the following examples.

Historically, there are many examples of material substitutions with concomitant improvement in worker safety. Classic examples include the substitution of the red phosphorous allotrope for the white. The latter ignites on contact with air and is thus a hazard for both direct burns to the worker and fire within the facility. The red allotrope is much more easily handled and does not present the same safety concerns. Another example is the substitution of phosphors for radium on watch dials. One early use for radioactive materials was on watch dials to allow them to be visible in the dark. Unfortunately, the workers painting these dials suffered from a series of radiation-induced ailments. This substitution improved the health of these workers immensely by reducing radiation exposure risk. The substitution of chlorinated solvents for petroleum naphthas in industry substantially reduced the fire hazard in cleaning operations. We must be careful in the selection of substitution materials, however, to ensure that one hazard is not being replaced by another.

Engineering Controls

Engineering controls invoke the application of mechanical solutions in an effort to reduce exposure to hazards. Engineering controls can be broadly grouped into the following categories: isolation and ventilation.

Isolation. Some processes cannot be changed, nor can the intrinsic risk associated with the process be reduced. In these cases, the only real alternative is to remove the worker from direct contact with the process. This is called *isolation*. As the name would suggest, isolation involves placing some type of barrier between the workers and the hazard to which they might otherwise be exposed. These barriers can be *physical*, a wall or simply distance between the worker and the hazard, or *temporal*, a process that operates when the worker is not present until it is complete. Some equipment is inherently dangerous due to the need for large amounts of energy to run it. Examples include high-pressure hydraulic lines, rotating machinery, and cutting blades. Because of the nature of the processes involved (e.g., moving heavy machinery and cutting metals), there is a significant potential for severe injury. Isolation offers a major reduction in risk. A physical barrier, a fence, enclosing rotating parts in metal, or isolating high-pressure hydraulic lines offers a good solution. Workers are not afforded an opportunity to come into contact with the dangerous equipment.

Certain operations, such as heat treating or cutting and drilling, cannot be nonhazardous. A heat-treating process requires elevated temperatures at the site of the work. These temperatures may be sufficient to burn on contact or may simply raise the ambient temperature to levels that surpass the body's ability to cope. Similarly, noise levels associated with a specific activity may be sufficient to cause permanent hearing loss either instantaneously or through long exposure. Isolation of the process (or the worker) may be the only feasible solution to such a problem.

Perhaps the easiest example to understand involves isolation from radiological or biological hazards. Highly radioactive materials, such as those found in nuclear research facilities, power plants, and medicine, often require a thick shield to prevent workers from receiving dangerous levels of exposure. The process itself may be isolated in such cases and workers only allowed to interact by remote control or with robotic devices.

Ventilation. In many occupational settings, the principal hazard is air contamination. Examples have been discussed previously and include exposure to dusts, vapors, metal fumes, and biological contaminations. It is often most convenient to reduce the hazard to the worker by supplying fresh, clean air. This is a direct application of the old adage "the solution to pollution is dilution." Ventilation may be concisely defined as the removal of contaminated air, the introduction of clean air, or both, in an effort to dilute a physical or chemical hazard to some acceptable level. Ventilation systems are often divided into two large categories, though significant overlap exists between these two rubrics. These are (1) local exhaust and supply ventilation and (2) general exhaust ventilation.

1. *Local exhaust and supply ventilation*. Often in industrial facilities, sources of air contamination are somewhat isolated by the process itself. Dust may be generated by a sanding and grinding operation that is limited to a single department or even a single machine. Organic vapors may be associated with a single degreasing tank. A biological hazard may exist at only one laboratory bench. In such cases, it makes sense to treat the source of the contamination directly. If the source area could be partially enclosed (thus isolating the process) and the contaminating material removed before it permeates the area, risk to the workers in general could be substantially reduced. This solution is quite effective both in a risk-reduction sense and in an economic sense. Exhaust systems can be designed with capture efficiencies approaching 100% for small areas.

2. *General exhaust ventilation*. While local exhaust and supply ventilation can be very efficient if sources of contamination within a facility are relatively isolated, they are not an effective solution if sources are dispersed throughout the facility. For example, a foundry may have multiple sources of particulate matter of various types and indeterminate generation patterns. Local exhaust ventilation methods are not appropriate in such circumstances; it is necessary to rely on general ventilation within the entire faculty to reduce risk to workers. General exhaust ventilation works much the same way as local exhaust ventilation except that now the entire facility is viewed as the "local" source. Large air-moving devices actively exhaust the contaminated air from within the building and supply fresh, outdoor air in its place. Such systems are costly in terms of capital outlay and in terms of heating and air-conditioning needs for the facility. However, if this situation is as described with numerous dispersed sources of contamination, risk reduction for workers often cannot be effected in any simpler or more cost-effective way.

Administrative Controls

Administrative controls, in which policies and procedures are implemented that reduce worker risk, have historically been the purview of management, but more recently cooperation between management and workers has made these more effective. Administrative controls include education of both management and the workforce on the risks experienced by the worker. While the education of the worker may seem obvious, as he needs to be aware of hazards and take proper steps to reduce them, the role of management may seem less obvious. Yet the role of management may be even more important than the role of the worker in implementing and maintaining a safe working environment. One administrative control that requires an understanding of the mode of toxicity and careful thought about dose-response relationships is the notion of "employee rotation," in which the employer may seek to subject a greater number of workers to the hazard for a shorter amount of time by rotating different workers through the high-exposure task over time. For some hazards (some acute hazards and some physical hazards) this type of "spreading the risk" is appropriate. However, for carcinogens and other hazards for which the risk accumulates

with exposure, OSHA and the occupational safety and health community generally oppose this strategy because if the toxicant has no threshold, all rotation does is spread the same amount of risk over more workers, widening the UCL of how many workers might be harmed. On the other hand, if the toxicant does have a true biological threshold, exposure-spreading might actually be sensible (assuming we could accurately estimate the threshold level and keep accurate track of each worker's cumulative exposure).

Personal Protective Equipment

Even when all of the above procedures are implemented, there may still be significant residual risk for workers. Some industrial processes, such as cleaning solvent tanks or handling radioactive material or chemical hazards, are intrinsically hazardous and cannot be made hazard-free. Under these conditions, one is forced to examine the use of *personal protective equipment* (PPE), a form of worker isolation, as a final choice in protecting the worker. Simple examples include the use of safety shoes to reduce foot injuries in occupational settings, and the use of hearing protection in settings where noise is excessive. In areas subject to high levels of air contamination, the use of respirators may be necessary. Respirators supply clean breathing air to the worker and range from simple filters that remove excess dust or organic vapors from the air to more complex apparatus that supply air to a worker entering an enclosed space that might not have sufficient oxygen to sustain life or that might be subject to concentrations of toxic gases high enough to cause injury. For extremely hazardous work in which any contact with the environment comes with substantial risk, full-body protection, sometimes referred to as moon suits, may be required. Such PPE protects the entire body from inhalation exposure, ingestion exposure, and dermal exposure. Such protection is used under the most hazardous of conditions – circumstances where biological, chemical, or other hazards are so great that any contact with the environment might prove harmful.

OSHA allows employers to control workers' exposures to chemicals by using respiratory protection when they can show that in a given operation, it is infeasible for engineering controls alone to

BOX 12.5 CONTROLS, PROFIT, EMPLOYMENT, AND HEALTH

Adam M. Finkel

With the advent of OSHA in the 1970s, the bottom-line operating costs for a facility could be markedly affected by fines and shutdowns. Management often took an adversarial position with respect to OSHA regulations, as well as with respect to organized workers or workers in general. This attitude has changed in the last 35 years. Astute managers have become aware of the potential to reduce workers' compensation premiums to increase productivity and to reduce training costs through the implementation of sensible workplace risk-reduction measures. It is now quite common to see a partnership between management and workers to develop education programs designed to make workers aware of the hazards in a workplace and to take ownership of their own safety and health. OSHA has taken a leadership role in this process as well through the implementation of its voluntary protection program (VPP), whereby facilities that go through rigorous training and evaluation procedures are allowed to reduce the likelihood and scope of OSHA inspections required. Such cooperative interaction is the hallmark of effective administrative control programs, ensuring safe workplaces and more productive facilities.

More broadly, the relationship between regulatory costs, especially the costs of OSHA regulations, and unemployment is controversial but important to consider as society seeks to further reduce occupational injury and illness. Unemployment and loss of income, after all, is itself risky and can lead to morbidity and mortality. However, in addition to the various studies (see above) suggesting that the costs of regulation are frequently exaggerated, recent scholarship tends to agree that regulations rarely "kill" significant net numbers of jobs (Coglianese et al. 2015). Regulations do, however, often create jobs in one sector while eliminating them in another, so it is important for policymakers to examine whether small net changes in employment mask significant economic and health effects on individuals who cannot find re-employment in the growing sectors of industry.

achieve a PEL (or when there is a TLV but no PEL, as part of the employer's General Duty). OSHA revised its respiratory protection standard (29 CFR 1910.134) in 1998, and in 2006 added a table of Assigned Protection Factors (APFs) based on the ability of each broad class of respirator (e.g., filtering facepiece or "dust mask," elastomeric cartridge respirator, powered air-purifying respirator or "PAPR," supplied-air hood) to reduce the concentration of a particle or vapor outside the respirator

BOX 12.6 INFORMATION DISCLOSURE: AN IMPORTANT AND FREE-STANDING PART OF THE HIERARCHY

Adam M. Finkel

Some controls to reduce occupational hazards rely on the simple power of knowledge. Information disseminated by the government, or disclosed by employers, can serve to empower workers to better understand and better protect themselves, or to help companies gauge and improve their performance, or in some cases to alert employers to the downsides of non-compliance with regulations and other norms. The power of information can be brought to bear at any level in the hierarchy of controls.

Perhaps the best example of the first type of information-as-solution involves OSHA's Hazard Communication Standard (29 CFR §1910.1200), often known as "HazCom," which since 1983 has given workers crucial understanding of the substances they may encounter in their workplaces, the health risks they pose, and the ways to reduce their exposures and risks. The cornerstone of the HazCom rule is the "Safety Data Sheet" (SDS; formerly known as the MSDS, or Material Safety Data Sheet), which is a resource for companies and workers that is supposed to fully disclose all of the health and safety hazards of a given substance, how to control them, and how to recognize and treat symptoms of acute or chronic overexposure. For much of the past 40 years, citations for not having SDSs accessible to workers have been among the most frequently issued OSHA citations, although the agency does not nearly as often cite manufacturers for disseminating incomplete or inaccurate data sheets. In 2012, OSHA amended HazCom to align with the newer United Nations Globally Harmonized System of Classification and Labeling of Chemicals, while retaining most or all of the substantive requirements of the existing rule.

OSHA often produces guidance documents and other informational material designed to help employers understand how (and why) to comply with workplace standards (for one listing of some of this voluminous material, see https://www.osha.gov/topics/text-index). But OSHA also requires in some cases that employers themselves disclose information that could help all companies better understand trends in workplace conditions. In particular, for several years, OSHA required large employers not only to post on-site annual summaries of the serious injuries that occurred at their facility (including calculating the injury rate per 100 employee-years of work) but also to electronically transmit the log and data to OSHA for analysis. That 2016 rule was rescinded in 2019 but was brought back into force in early 2022.

A third type of useful information relies on the power of deterrence. Beginning in the Obama administration (but again, rescinded in the subsequent administration), OSHA greatly increased its use of press releases, targeted at local media, explaining why a particular company had just received a major civil penalty for one or more violations of OSHA standards. OSHA had always issued occasional press releases for total fines of several hundred thousand dollars or more but began issuing them for total penalties of $40,000 or more, which increased the total number of releases nationwide from roughly 150 per year to nearly 500 per year. The rationale behind this initiative was that corporate leadership may well care much more about the possible effect on their stock price of documenting their lapses. However, the policy was also criticized for two main reasons: (1) in some cases, articles were written based on penalties proposed by OSHA that were later negotiated downward, and (2) using the dollar amount as the sole criterion means that a facility with one serious lapse would be publicized, while one with dozens of less serious ones might not. Ultimately, the deterrent effect of OSHA's policy received a major validation in a study by Johnson (2020), who demonstrated that after press releases were issued, future violations at all similar facilities within 5 km of the subject facility went down by more than 70%. Johnson concluded that a single press release could have a similar deterrent effect as more than 200 on-site OSHA inspections would have had.

to a lesser concentration. OSHA defines the "Maximum Use Concentration" as the APF multiplied by the PEL; for example, if the PEL for a given contaminant is 20 ppm, and the employer provides a respirator with an APF of 10, the employee can wear that respirator in an atmosphere containing 200 ppm of the substance and be in compliance with the OSHA standard.

THE EVOLUTION OF INDUSTRIAL HYGIENE AND THE ROLE OF NEW PROFESSIONALS

Historically, industrial hygiene (or occupational hygiene) has focused on worker exposures to a single contaminant such as specific solvents, nuisance dusts, or radiation. However, recent studies in epidemiology, toxicology, and pharmacokinetics indicate that such a focus may be too narrow. Health outcomes are likely associated with multiple exposures over a lifetime to compounds that may act as synergists or promoters of disease. To address the complex workplaces of today, the profession of industrial hygiene is changing. New professionals in the field must now have broad-based knowledge of the mechanisms of contaminant action. They must study biology, toxicology, epidemiology, and other related sciences. The "new industrial hygienist" must be aware of the compounding effects from, for example, exposure to various related solvents or classes of pesticides, some of which accumulate in the body over the lifespan of the worker. Thus, an understanding of the historical exposures experienced by workers is also necessary. The metabolism of compounds that enter the body must be understood as well; fast-metabolizing compounds may produce toxic metabolites, and slow-metabolizing compounds may accumulate in body-storage compartments and cause health problems years after exposure.

Those aspiring to become industrial hygienists in the twenty-first century must become more general in their education and in their work aspirations. In the coming years, industrial hygienists will still be required to "know their instrumentation" and be able to take samples in the field. But they will also need to be aware of secondary exposures experienced by workers in their nonwork activity, as well as the impact of the industrial environment on the surrounding community. Consistent with the NIOSH Total Worker Health® (TWH) model and program, changes to the workplace (e.g., nonstandard work arrangements and the gig economy), and the demographics of the workforce (e.g., older workers and an increasing prevalence of chronic disease among the employed) warrant a more comprehensive and holistic approach to protecting and promoting worker safety and health. The TWH approach integrates traditional occupational safety and health in the workplace with concerns about overall worker well-being, both within and outside of work. Through academic training, continued professional development, and collaboration across disciplines, current and future occupational health and safety professionals will greatly benefit from an expanded set of skills and knowledge to meet the demands of a changing working environment (Schulte et al., 2019).

EMERGING HAZARDS

Today, workers continue to experience many of the same historical hazards in the workplace, but there are also new hazards to contend with – engineered nanomaterials, the adverse effects of artificial intelligence, psychosocial hazards etc. And new and unanticipated hazards are still likely to emerge. Often, the hazards are not evident at first, as with radiation and asbestos, but come to light only after workers have received exposures long and significant enough to develop the clinically evident disease. We hope not to repeat some of the mistakes of the past. Let us examine some emerging concerns to make ourselves aware of the possibilities of worker injury and disease.

Nanotechnology

Nanotechnology, the use of very small, even molecular-scale, machines, may well be the principal advance of the 21st century and have a variety of uses across many industries – from food production, to coatings, to cosmetics and industrial processes. There is potential for worker harm from exposure to nanomaterials, which, if inhaled, tend to settle deeper in the lung and can be transported to remote areas of the body to cause health impacts. Now is the time to examine such exposures and refine methods of protecting workers from inadvertent injury and illness in the nanotechnology workplace (Service 2005).

Impact of Climate on Workers

There are many health and safety considerations associated with extreme weather events that have a significant impact on workers, particularly those who spend considerable time working outdoors. The effects can be direct, such as heat stroke or even death resulting from working in hot conditions for prolonged periods of time. Extreme weather can also indirectly affect the health

and safety of workers, as changes in precipitation and temperature can impact the concentrations of ambient air pollution as well as the prevalence of biological hazards including vector-borne diseases.

Changes in climate have also contributed to an increase in the frequency and severity of wildfires, resulting in a growing concern not just for the health and safety of wildland firefighters but for all outdoor workers potentially exposed to smoke from wildfires. Three states significantly impacted by wildfires – California, Oregon, and Washington – have recently issued rules to protect workers from wildfire smoke: https://www.cdc.gov/niosh/topics/firefighting/wffsmoke.html. These rules include requirements for employers to provide training, implement engineering or administrative controls, and provide or even require respirator use, depending on the level of the US Environmental Protection Agency's air quality index (AQI) for PM2.5, a primary component of wildfire smoke. As the AQI is linked to the National Ambient Air Quality Standards that are established to protect public health, the actions of these states would seem to constitute a tacit acknowledgment that occupational standards for respirable particulate matter, exposures to which rarely occur in isolation, do not adequately protect the health of workers.

New Industrial Processes

New industrial processes are being developed constantly. Consider that integrated circuits and the concomitant assembly technology have all been developed in the last 50 years. New processes such as genetic engineering, related biotechnologies, and advanced manufacturing techniques (e.g., 3D printing) are likely to be developed more fully in the next 25 years. We must consider the impact on the health of workers who engage in these industrial activities. Are they at risk for certain known diseases? Are there new diseases that will emerge from these new processes? Some industrial processes will be common 25 years from now that are not even known at this point. How will we set up a mechanism that affords adequate protection to evaluate the impact on workers of these new processes? For a very recent example of a modern hazard only becoming known as a cause of serious occupational disease years after exposures began, see the literature on the relationship between diacetyl (used in artificial butter flavoring) and "popcorn lung disease" (*bronchi olitis obliterans*) (see, e.g., Schneider 2006).

BOX 12.7 REPEATED HEAD TRAUMA

Adam M. Finkel

Evidence has emerged over the past decade (although the risk had been suspected and written about for more than a century) that multiple concussions, along with "subconcussive" impacts, are strongly associated with the development of a grave neurodegenerative disease now generally called chronic traumatic encephalopathy (CTE), for chronic traumatic encephalopathy (Baugh et al. 2012). Head trauma poses fascinating problems for occupational safety and health professionals: (1) it is both an injury and the apparent cause of a serious illness; (2) the illness can affect more than the worker (prominent reports exist of professional athletes who harmed others while suffering the cognitive and behavioral effects of CTE); (3) repetitive head trauma is both an occupational (professional sports, logging, military service, commercial driving, etc.) and a frequent nonoccupational exposure; (4) some of the entertainment and sports occupations where head trauma is most prominent are clearly under OSHA's jurisdiction but are not typical scenes of OSHA inspection or regulation; (5) PPE may not be helpful in this case, as the damage accrues when the human brain impacts the inside of the skull, not from the initial impact per se. The Harvard Football Players Health Study (Finkel et al. 2018) wrote a comprehensive analysis of how OSHA could help to reduce CTE risks in workplaces, discussing various informational, partnership, General Duty Clause enforcement, and standard-setting options that might provide some relief to workers, and by extension to college athletes et al not covered by OSHA. Interestingly, the most important court case further establishing that the OSH Act gives OSHA jurisdiction over sports and entertainment as well as manufacturing and service industries involved the 2014 case of *SeaWorld v. DOL*, where OSHA levied fines against a water park for allowing trainers to work in the water with an orca who had previously killed trainers at other parks.

BOX 12.8 NIGHT SHIFT WORK AND BREAST CANCER RISK

Mingzhu Fang

All types of organisms possess natural, internal circadian rhythms that are adjusted to the local environment by external cues, including light, nutrients, and temperature. In humans, the central clock, which is located at the suprachiasmatic nucleus of the hypothalamus, receives light signals through the eyes to adjust the internal circadian rhythm to the 24-hour light-dark cycle of the solar day. The central clock also synchronizes circadian rhythms across most peripheral organs and cells via endocrine (e.g., melatonin) and neural pathways. Therefore, our body systems are adapted to the 24-hour solar day at the behavioral, biochemical, physiological, and cellular and molecular levels.

Circadian disruption is defined as internally or externally induced acute or chronic temporal disorganization and misalignment of the time structure in living systems. Specifically, circadian disruption occurs when the daily circadian rhythms in our bodies are not adjusted to the environmental light-dark cycle and/or are no longer coordinated with each other. Excessive exposure to light at night (LAN), persistent night shift work, jet lag, and sleep deprivation can cause circadian disruption. Long-term circadian disruption causes chronic diseases, including cancer and metabolic syndrome.

Recent survey data indicate that greater than 27% of employees are working alternative shifts and that 7%–20% of workers in occupations, such as the protective services, healthcare, production, and transportation are working at night. Night shift work causes a complex exposure scenario, involving exposure to electric LAN, sleep disturbances, meal time changes, and social stressors. In most health outcome studies, exposure assessments of night shift work are mainly based on lifestyle and occupational surveys and/or daily activity diaries. The information provided in the surveys and diaries are reviewed, and the sleep time, amount, and quality are assessed for each subject. Outdoor LAN exposures are measured with time-varying satellite data analysis, whereas indoor LAN exposures are usually measured using light intensity data loggers. In contrast, only a limited number of studies have measured personal light exposures in shift workers in various exposure scenarios. Recently developed medical devices, such as Actigraph, can monitor light exposure and activity, which can be used to assess circadian rhythms accurately in individuals over an extended period of time.

Earlier epidemiological studies in shift workers indicate that nurses and pilots have an increased risk of cancer, especially in breast and prostate, respectively. Results from an occupational cohort study showed an increased risk of breast cancer among women who worked long-term (for 10 or more years) night shift, especially those who worked the night shift for more than 20 years. A similar conclusion has been made by an analysis of data from Nurses' Health Study cohorts with 24-year follow-up for total 9,541 incident cases of invasive breast cancer. These studies found a significantly increased risk of breast cancer in women with 20 years or more of night shift work, particularly among women who began night shift work in early adulthood (before age 30). In a pooled analysis of five European case-control studies of night shift work and breast cancer incidence, night shift work was positively associated with increased breast cancer risk in premenopausal women. In these studies, women who worked the night shift with high intensity (at least three times/week) for more than 20 years were at the highest risk, and the associations were strongest in women with hormone receptors positive (i.e., ER+ and ER+/HER2+) breast cancer subtypes.

Laboratory animal studies have also provided compelling evidence for the carcinogenicity of altered light-dark schedules in various organs (e.g., breast and liver) of rodents. Chronic exposure to constant light increased the incidence of carcinogen-induced mammary tumors in female rats. Moreover, long-term exposure to a jet-lag protocol mimicking rotating shift work, accelerated the growth of xenograft breast cancer in immune-deficient mice. Furthermore, chronic jet lag advanced tumor onset and accelerated tumor growth in breast cancer-prone transgenic mice and conditional p53 mutant mice.

These human and animal data together with mechanistic study results prompted the International Agency for Research on Cancer to classify night shift work as *probably carcinogenic to humans* (Group 2A) (IARC 2010; IARC 2020). A recent National Toxicology Program cancer hazard assessment report concluded that persistent night shift work that disrupts circadian rhythms can cause breast cancer in women and may cause prostate cancer in men (NTP 2021).

REFERENCES

International Agency for Research on Cancer (IARC). 2010. "Painting, Firefighting, and Shiftwork." IARC Monographs on the Identification of Carcinogenic Hazards to Humans Volume 98. IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS. Lyon, France. https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Painting-Firefighting-And-Shiftwork-2010

International Agency for Research on Cancer (IARC). 2020. "Night Shift Work." *IARC Monographs on the Identification of Carcinogenic Hazards to Humans Volume 124*. IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS. Lyon, France. https://publications.iarc.fr/593

National Toxicology Program (NTP). 2021. "NTP Cancer Hazard Assessment Report on Night Shift Work and Light at Night." NTP Review of Shift Work at Night, Light at Night, and Circadian Disruption. https://ntp.niehs.nih.gov/ntp/results/pubs/cancer_assessment/lanfinal20210400_508.pdf

Exposure to Mixtures

Historically, risk assessors have focused on one hazard at a time, even though we know that workers are exposed to multiple hazards on the job. For example, pharmaceutical manufacturers use a variety of compounds in the synthesis of their products; electronics industries use a large amount of silicon but dope the surfaces with different trace elements to build circuitry with specific properties. Understanding the effects of these mixtures of compounds is the main need for future industrial hygienists (Fox et al. 2018; Lentz et al. 2015). The task is not easy. How will these mixtures be measured? How will the components be weighted with regard to health outcomes? Are there compounds that interact synergistically to produce a large effect on health while each individually produces none? This is the challenge of the future.

Technological Change

Overall, the role of the future hygienist is to adapt to the technological change that is certain to come, while "holding the fort" against hazards known for decades or more, where continued vigilance is necessary to provide workers with a fighting chance to return home safely each day.

THOUGHT QUESTIONS

1. What are the most important aspects of occupational risk assessment methodology that tend to make risk estimates *conservative* (prone to overestimation), and which aspects work in the opposite direction? On balance, do you think OSHA risk assessment errs on the side of precaution too much or not enough?
2. What are the most significant hazards identified in recent years that have been insufficiently characterized or addressed by the occupational safety and health community? What new hazards would you urge OSHA or NIOSH to pay more attention to in the immediate future?
3. How can society reliably assess the contribution of specific interventions (e.g., regulations, enforcement, partnerships) to observed changes in measured results (fatalities, injuries, illnesses) given the difficulty in knowing what changes might have occurred in the absence of the interventions?
4. Given the many procedural and analytic challenges inherent in researching and regulating occupational safety and health risks, and the considerable overlap between community and workplace exposures, what would the merits and pitfalls be of creating a single agency with jurisdiction over both environmental and occupational risks?

DISCLAIMERS

The findings and conclusions in this chapter are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. Throughout this chapter, particularly in the online interactive version, additional material is provided in boxes. This material was assigned by the editors and does not necessarily represent the views of the chapter authors or of NIOSH.

Some material in the 2007 version of this chapter was originally contributed by P. Barry Ryan.

REFERENCES

American Textile Manufacturers Institute et al. v. *Donovan, Secretary of Labor et al*., No. 79-1429 (1981).

Annas, G. J. 1981. "Blue Jeans for You, Brown Lung for Us": OSHA's Cotton Dust Standard. *Hastings Center Report*, 11: 15–16.

Ashford, N. A., and Caldart, N. A. 1996. *Technology, Law, and the Working Environment* (rev. ed.). New York: Island Press.

Baker, E. L., Jr., et al. 1979. Occupational Lead Poisoning in the United States: Clinical and Biochemical Findings Related to Blood Lead Levels. *British Journal of Industrial Medicine*, 36(4): 314–322.

Baker, E. L., Jr., et al. 1985. The Neurotoxicity of Industrial Solvents: A Review of the Literature. *American Journal of Industrial Medicine*, 8(3): 207–217.

Barstow, D. 2003, December 22. U.S. Rarely Seeks Charges for Deaths in Workplace. *New York Times*, p. A1.

Baugh, C. M., et al. 2012. Chronic Traumatic Encephalopathy: Neurodegeneration following Repetitive Concussive and Subconcussive Brain Trauma. *Brain Imaging and Behavior*, **6**: 244–254.

Bufton, M. W., and Melling, J. 2005. "A Mere Matter of Rock": Organized Labour, Scientific Evidence and British Government Schemes for Compensation of Silicosis and Pneumoconiosis Among Coalminers, 1926–1940. *Medical History*, 49(2): 155–178.

Bureau of Labor Statistics. 2004. *Census of Fatal Occupational Injuries, 1992–2004*. Washington, DC: U.S. Department of Labor.

Bureau of Labor Statistics. 2022, April 1. Economic News Release Employment Situation Tables A-1 and A-9. https://www.bls.gov/news.release/empsit.toc.htm. Accessed May 2, 2022.

Burmaster, D. 2000. Distributions of Total Job Tenure for Men and Women in Selected Industries and Occupations in the United States, February 1996. *Risk Analysis*, 20(2): 205–224.

Cordaro, T. L. 2015. Recent OSHA Inspection Statistics and Enforcement Initiatives. *JacksonLewis OSHA Law Blog*, https://www.oshalawblog.com/2015/03/articles/recent-osha-inspection-statistics-and-enforcement-initiatives/

Chemical Week. 1976, September 15. Polyvinyl Chloride Rolls out of Jeopardy, Into Jubilation, p. 34.

Cherniack, M. 1986. *The Hawk's Nest Incident: America's Worst Industrial Disaster*. New Haven, Conn.: Yale University Press.

Coglianese, C., Finkel, A., and Carrigan, C. 2015. *Does Regulation Kill Jobs?* University of Pennsylvania Press. https://www.law.upenn.edu/institutes/ppr/doesregulationkilljobs/

Corn, J. K. 1981. Byssinosis: An Historical Perspective. *American Journal of Industrial Medicine*, 2(4): 331–352.

Darby, S., Hill, D., and Doll, R. 2001. Radon: A Likely Carcinogen at All Exposures. *Annals of Oncology*, 12: 1341–1351.

Environmental Protection Agency. 1992. Draft Report: A Cross-Species Scaling Factor for Carcinogen Risk Assessment Based on Equivalence of $mg/kg^{3/4}$/day. *Federal Register*, 57(109): 24152–24173.

Environmental Protection Agency. 1999, June 17–18. Common-Sense Approaches to Protecting Workers and the Environment: Interagency Cooperation Towards Cooperative Solutions. *Conference Held in Washington, D.C.*

Environmental Protection Agency. 2000. EPA/OSHA Advisory on 2,4-Dichlorophenol. http://epa.gov/oppt/pubs/24dcp.htm.

Environmental Protection Agency. 2004. Toxic Substances Control Act, Section 8(e). http://www.epa.gov/opptintr/tsca8e/pubs/facts8e.htm.

Environmental Protection Agency. 2006a. Development of Acute Exposure Guideline Levels. http://www.epa.gov/oppt/aegl.

Environmental Protection Agency. 2006b. Region 8: Libby Asbestos. http://www.epa.gov/region8/superfund/libby/background.html.

Federal Advisory Committee Act Amendments. 2006. U.S.C. 5 App. (as amended). http://www.usdoj.gov/04foia/facastat.pdf.

Finkel, A. M. 2005, December. Kilo-Disparities? Prevailing Concentrations of Carcinogenic Air Pollutants in U.S. Workplaces and the Ambient Environment. *Paper Presented at the Annual Meeting of the Society for Risk Analysis*, Orlando, FL.

Finkel, A. M. 2008, September 16. There Is No "War" on Occupational Cancer. *Presentation before the President's Cancer Panel*, New Brunswick, NJ. https://healthandenvironment.net/uploads-old/No%20War%20on%20Occupational%20Cancer-%20Finkel.doc

Finkel, A. M., Deubert, C. R., Lobel, O., Cohen, I. G., and Lynch, H. F. 2018. The NFL as a Workplace: The Prospect of Applying Occupational Health and Safety Law to Protect NFL Workers. *Arizona Law Review*, **60**: 291–368.

Fox, M. A., Spicer, K., Chosewood, L. C., Susi, P., Johns, D. O., and Dotson, G. S. 2018. Implications of Applying Cumulative Risk Assessment to the Workplace. *Environment International*, 115: 230–238.

Gochfeld, M. 2005. Chronologic History of Occupational Medicine. *Journal of Occupational and Environmental Medicine*, 47(2): 96–114.

Gomez, M. R. 1991. Validation of Sampling Data from the Occupational Safety and Health Administration (OSHA) Integrated Management Information System (IMIS). *American Industrial Hygiene Association Journal*, 52(9): A488.

Graham, J. D., and Wiener, J. B. 1995. *Risk Versus Risk: Tradeoffs in Protecting Health and the Environment*. Cambridge, MA: Harvard University Press.

Hattis, D., and Goble, R. L. 1991. Expected Values for Projected Cancer Risks from Putative Genetically Acting Agents. *Risk Analysis*, 11(3): 359–363.

The Histories of Herodotus, The Persian Wars, Book 7 Polymnia, c. 484–425 because n.d.

Hoang, A., Fagan, K., Cannon, D. L., et al. 2021. Assessment of Methylene Chloride-Related Fatalities in the United States, 1980–2018. *JAMA Internal Medicine*, 181(6): 797–805.

House Subcommittee on Workforce Protections. 2001, June 14. OSHA's Standard Setting Process. http://www.house.gov/ed_workforce/hearings/107th/wp/osha61401/seminario.htm.

Islam, K. M., and Anderson, H. A. 2006. Status of Work-Related Diseases in Wisconsin: Five Occupational Health Indicators. *Wisconsin Medical Journal*, 105(2): 26–31.

Johnson, J. M. 2001. A Review and Synthesis of the Costs of Workplace Regulations. (Working Paper) Arlington, VA: Regulatory Studies Program, Mercatus Center, George Mason University.

Johnson, M. S. 2020. Regulation by Shaming: Deterrence Effects of Publicizing Violations of Workplace Safety and Health Laws. *American Economic Review*, 110(6): 1866–1904.

Jones, J. H. 1981. Worker Exposure to Vinyl Chloride and Polyvinyl Chloride. *Environmental Health Perspectives*, 41: 129–136.

Kniesner, T. J., Leeth, J. D. 1995. Numerical simulation as a complement to econometric research on workplace safety. *J Risk Uncertainty* 10, 99–125. https://doi.org/10.1007/BF01083555

Kuempel, E. D., Sweeney, L. M., Morris, J. B., and Jarabek, A. M. 2015. Advances in Inhalation Dosimetry Models and Methods for Occupational Risk Assessment and Exposure Limit Derivation. *Journal of Occupational and Environmental Hygiene*, 12: S18–S40.

Landrigan, P. J. 1987. Benzene and Leukemia. *American Journal of Industrial Medicine*, 11(5): 605–606.

Landrigan, P. J., et al. 1980. Clinical Epidemiology of Occupational Neurotoxic Disease. *Neurobehavioral Toxicology*, 2(1): 43–48.

Lavoue, J., Friesen, M. C., and Burstyn, I. 2013. Workplace Measurements by the US Occupational Safety and Health Administration since 1979: Descriptive Analysis and Potential Uses for Exposure Assessment. *Annals of Occupational Hygiene*, 57(1): 77–97.

Leigh, P., et al. 1997.Occupational Injury and Illness in the United States: Estimated Costs, Morbidity, and Mortality. *Archives of Internal Medicine*, 157: 1557–1568.

Leigh, J. P., Waehrer, G., Miller, T. R., and Keenan, C. 2004. Costs of Occupational Injury and Illness Across Industries. *Scandinavian Journal of Work, Environment & Health*, 30: 199–205.

Lentz, T. J., Dotson, G. S., Williams, P. R. D., Maier, A., Gadagbui, B., Panadalai, S. P., et al. 2015. Aggregate Exposure and Cumulative Risk Assessment – Integrating Occupational and Non-Occupational Risk Factors. *Journal of Occupational and Environmental Hygiene*, 12:Suppl. 1: S112–S126.

Levine, D. I., Toffel, M. W., and Johnson, M. S. 2012. Randomized Government Safety Inspections Reduce Worker Injuries with no Detectable Job Loss. *Science*, 336: 907–911.

Lowell Center for Sustainable Production. 2006. *Integration of Occupational and Environmental Health*. Lowell, MA: University of Massachusetts. http://sustainableproduction.org/proj.inte.abou.shtml.

McMichael, A. J. 1976. Standardized Mortality Ratios and the "Healthy Worker Effect": Scratching Below the Surface. *Journal of Occupational Medicine*, 18: 165–168.

National Academy of Sciences. 1983. *Risk Assessment in the Federal Government: Managing the Process*. National Academy Press: Washington, DC, https://nap.nationalacademies.org/catalog/366/risk-assessment-in-the-federal-government-managing-the-process

National Institute for Occupational Safety and Health. 2020.*Current Intelligence Bulletin 69: NIOSH Practices in Occupational Risk Assessment*. By Daniels, R. D., Gilbert, S. J., Kuppusamy, S. P., Kuempel, E. D., Park, R. M., Pandalai, S. P., Smith, R. J., Wheeler, M. W., Whittaker, C., Schulte, P. A. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 2020-106 (revised 03/2020). https://doi.org/10.26616/NIOSHPUB2020106revised032020.

NIOSH. 2016. *Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione*. By McKernan, L. T., Niemeier, R. T., Kreiss, K., Hubbs, A., Park, R., Dankovic, D., Dunn, K. H., Parker, J., Fedan, K., Streicher, R., Fedan, J., Garcia, A., Whittaker, C., Gilbert, S., Nourian, F., Galloway, E., Smith, R., Lentz, T. J., Hirst, D., Topmiller, J., Curwin, B. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2016-111.

NIOSH. 2016a. *Current Intelligence Bulletin 68: NIOSH Chemical Carcinogen Policy*. By Whittaker C, Rice F, McKernan L, Dankovic D, Lentz TJ, MacMahon K, Kuempel E, Zumwalde R, Schulte P, on behalf of the NIOSH Carcinogen and RELs Policy Update Committee. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2017-100.

National Toxicology Program. 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 2-Bromopropane (2-BP). NTP-CERHR MON, 10, i–III11.

Recommend including the NIOSH Occupational Risk Assessment Document: n.d. https://www.cdc.gov/niosh/docs/2020-106/default.html

Occupational Safety and Health Administration. 1997, January 10. Occupational Exposure to Methylene Chloride. *Federal Register*, 62(7).

Occupational Safety and Health Administration. 2019. Chemical Exposure Health Data. Datafile "Inspection_NAICS_CY19b.csv," containing information on 41,850 samples taken during calendar year 2019. https://www.osha.gov/opengov/health-samples.

Office of Technology Assessment. 1995, September. Gauging Control Technology and Regulatory Impacts in Occupational Safety and Health: An Appraisal of OSHA's Analytic Approach (Report #OTA-ENV-635).

Pandanell, M. 2005. The Texas City Disaster: April 16, 1947. 2005. http://www.local1259iaff.org/disaster.html.

Piltingsrud, H. V., Zimmer, A. T., and Rourke, A. B. 2003. The Development of Substitute Inks and Controls for Reducing Workplace Concentrations of Organic Solvent Vapors in a Vinyl Shower Curtain Printing Plant. *Applied Occupational and Environmental Hygiene*, 18(8): 597–619.

Pratt, S. G., Kisner, S. M., and Helmkamp, J. C. 1996. Machinery-Related Occupational Fatalities in the United States, 1980 to 1989. *Journal of Occupational and Environmental Medicine*, 38(1): 70–76.

Rhomberg, L. R. 1997. A Survey of Methods for Chemical Health Risk Assessment Among Federal Regulatory Agencies. *Human and Ecological Risk Assessment*, 3(6): 1029–1196.

Robinson, R. 2004. Bromopropane: Ozone-Sparing Solvent Is Neurotoxic (News from the Annual Meeting). *Neurology Today*, 4: 15–16.

Rosenman, K. D., et al. 2006. How Much Work-Related Injury and Illness Is Missed by the Current National Surveillance System? *Journal of Occupational and Environmental Medicine*, 48(4): 357–365.

Rosner, D., and Markowitz, G. 2020. A Short History of Occupational Safety and Health in the United States. *American Journal of Public Health*, 110: 622–628.

Ruttenberg, R. 2004, February. *Not Too Costly After All: An Examination of the Inflated Cost-Estimates of Health, Safety, and Environmental Protections*. Report prepared for Public Citizen Foundation Inc. https://www.citizen.org/wp-content/uploads/migration/not_too_costly.pdf.

Schneider, A. 2006, August 3. House Members Fault Agency for Inaction on Flavoring Peril. *Baltimore Sun*.

Schulte, P. A. 2017. An Approach to Assess the Burden of Work-Related Injury, Disease, and Distress. *American Journal of Public Health*, 107(7): 1051–1057.

Schulte, P. A., Delclos, G., Felknor, S. A., & Chosewood, L. C. 2019. Toward an Expanded Focus for Occupational Safety and Health: A Commentary. *International Journal of Environmental Research and Public Health*, 16(24): 4946.

Selikoff, I. J., and Greenberg, M. 1991. A Landmark Case in Asbestosis. *Journal of the American Medical Association*, 265(7): 898–901.

Selikoff, I. J., et al. 1965. The Occurrence of Asbestosis Among Insulation Workers in the United States. *Annals of the New York Academy of Sciences*, 132(1): 139–155.

Selikoff, I. J., et al. 1967. Asbestosis and Neoplasia. *American Journal of Medicine*, 42(4): 487–496.

Service, R. F. 2005. Related Nanotechnology: Calls Rise for More Research on Toxicology of Nanomaterials." *Science*, 310, 1609.

Sinclair, U. 1985. *The Jungle*. New York: Penguin. (Originally published 1906.)

Smith, B. E. 1981. Black Lung: The Social Production of Disease. *International Journal of Health Services*, 11(3): 343–359.

Stout, N. A., and Linn, H. I. 2002. Occupational Injury Prevention Research: Progress and Priorities. *Injury Prevention*, 8(supp. 4): 9–14.

Sunstein, C. R. 1996. Health-Health Tradeoffs. Chicago Working Papers in Law and Economics, no. 42.

Takala, J., Hämäläinen, P., Saarela, K. L., et al. 2014. Global Estimates of the Burden of Injury and Illness at Work in 2012. *Journal of Occupational and Environmental Hygiene*, 11(5): 326–337.

Tamers, S. A., et al. 2020. Envisioning the Future of Work to Safeguard the Safety, Health, and Well-being of the Workforce: A Perspective from the CDC's National Institute for Occupational Safety and Health. *American Journal of Industrial Medicine*, 631: 1065–1084.

US Census Bureau. 2002, February. 2019 SUSB Annual Data Tables by Establishment Industry. https://www.census.gov/data/tables/2019/econ/susb/2019-susb-annual.html. Accessed May 2, 2022.

US District Court, District of New Jersey. *Adam M. Finkel v. U.S. Department of Labor, Civil Action No. 05-5525*, decided June 29, 2007. Opinion available at https://casetext.com/case/finkel-v-us-department-of-labor.

US EPA. 2017. Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, 82 FR 33726.

Upton, A. C. 1987. Prevention of Work-Related Injuries and Diseases: Lessons from Experience with Ionizing Radiation. *American Journal of Industrial Medicine*, 12(3): 291–309.

Urbina, I. 2013, March 30. As OSHA Emphasizes Safety, Long-Term Health Risks Fester." *New York Times*.

Vig, N., and Faure, M. G. (eds.). 2004. *Green Giants? Environmental Policies of the United States and the European Union*. Cambridge, MA: MIT Press.

Viscusi, W. K. 2013, October. Using Data from the Census of Fatal Occupational Injuries to Estimate the "Value of a Statistical Life". *Monthly Labor Review*, 1–16.

Von Drehle, D. 2003. *Triangle: The Fire That Changed America*. New York: Atlantic Monthly Press.

Winegar, D. A., et al. 1977. Chronic Occupational Exposure to Lead: An Evaluation of the Health of Smelter Workers. *Journal of Occupational Medicine*, 19(9): 603–606.

Yassin, A., Yebesi, F., and Tingle, R. 2005. Occupational Exposure to Crystalline Silica Dust in the United States, 1988–2003. *Environmental Health Perspectives*, 113(3): 255–260.

Young, R. C., Jr., and Rachal, R. E. 1996. Pulmonary Disability in Former Appalachian Coal Miners. *Journal National Medical Association*, 88: 517–522.