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Exposure assessment for a study of workers exposed to acrylonitrile

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Procedures used to develop estimates of exposure to acrylonitrile for a cohort study (>25 000 workers in 8 monomer, fiber, and resin companies from 1952 to 1983) are presented. Visits to the companies were made, interviews of workers were conducted, historical records were made, and measurements were taken. On the basis of similar tasks, locations, other exposures, and a similar distribution of exposures to acrylonitrile, 3600 exposure groups were formed. Special procedures were used to reduce the misclassification of workers performing tasks that varied in time but that were inadequately reflected in the job title. A software program organized and retained all exposure information on each exposure group. Quantitative estimates of acrylonitrile exposure were developed using a hierarchical approach in a software program that documented the derivation of each estimate and facilitated data review. Two of the estimation methods were evaluated in a comparison with measurement data.

Key terms cancer, occupation.

Quantitative assessment of exposures is a critical element in modern-day retrospective studies of occupational cohorts. This view reflects the recognition that quantitative exposure estimates are crucial for risk assessment, and it is a reflection of the greater availability of measurement data today than in the past. The procedures used to develop quantitative estimates are, however, not always well described (1) and therefore make it difficult to understand what procedures were used and also difficult to evaluate the quality of the exposure estimates.

This report provides a detailed description of the procedures used to develop quantitative estimates of occupational exposure to acrylonitrile for a study evaluating the mortality of workers exposed to acrylonitrile (2).

Background of the cohort

The cohort included all workers employed at least 1 day in 8 facilities located in Virginia, Ohio, Texas, Louisiana, Florida, and Alabama (N=25 460, of whom over 16 000 were exposed to acrylonitrile). Four facilities made acrylonitrile monomer, 3 made acrylic fiber, and 1 made acrylic resins. Small-scale production of other acrylonitrile products (adiponitrile, acrylamide) also occurred in some of the facilities. In addition, most of the facilities produced other nonacrylonitrile products, including polyester fibers, styrene, formaldehyde, and other chemicals. The year of start-up of the acrylonitrile operations in these companies ranged from 1952 to 1965.

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Plant visits

Three to 4 site visits of 3 to 4 days in length were made to each plant by the industrial hygienists of the study. The visits included a walk-through survey of the acrylonitrile production operations [defined as areas handling acrylonitrile or production areas where measured levels of acrylonitrile were ≥0.01 parts per million (ppm)] and interviews with long-term workers from these operations. All the acrylonitrile operations of the plant were carefully evaluated, including acrylonitrile-using or acrylonitrile-handling production operations, maintenance, shipping and receiving, quality control, research and development, environmental control, utilities, engineering, and industrial hygiene, safety and medical departments. Other departments were examined only briefly.

The initial site visit provided a general overview of the plant operations and job tasks. For the second visit, a questionnaire was developed to investigate each acrylonitrile department; it focused on widely held jobs (identified from the personnel records), their tasks, time spent at the tasks, anecdotal reports of adverse health effects, changes in engineering controls, administrative or work practices over time, and procedures for spills, upsets and other unusual occurrences. The participating companies requested that detailed questionnaires be developed to provide companies and unions with a clear indication of the information being sought. Use of a structured interview to obtain information was not successful, however. Recall by interviewees did not follow the questionnaire, and it quickly became obvious that the interviews were much more fruitful when they were free-flowing. Thereafter, the questionnaires served as a checklist to ensure that all topics were covered.

The study investigators identified long-term wage and salaried workers (generally >10 years) in the acrylonitrile-producing and using departments for interview from the abstracted personnel records. When subjects were unavailable due to retirement, vacation, or other types of absences, we asked the companies and unions (when present) to jointly select substitutes. The number of interviewees ranged from 2 to 5 for each department. Wage and salaried workers for a given department were interviewed separately, and the information obtained from the 2 groups was generally consistent. Consensus on exposure-related issues was generally obtained within each group, but it was not required. Where the information was not consistent and consensus could not be obtained, the most likely occurrence, as judged by the study investigators, was identified as having low confidence. Over 100 interviews were conducted in the first round of site visits alone. Historical records that could provide insight into earlier work conditions were obtained. A report was written that summarized the site visit for each plant and described the history of the plant operations, engineering changes, the major job titles and their duties, the reported health effects, and the measurements.

Description of the monitoring data

The companies provided all available monitoring data through the date of the site visit (N=18 000). The data from 6 of the companies were provided in electronic form; those from the other 2 companies were received in paper form and were computerized by the study investigators. Measurements of acrylonitrile levels were available from 1977 or 1978 for 7 of the 8 companies in the study (Zey JN, Stewart PA, Hornung R, Herrick R, Mueller CA, McCammon C, et al. Evaluation of side-by-side pairs of acrylonitrile personal air samples collected using different sampling techniques, unpublished results) and for 1 plant (a fiber plant) from 1960. The measurements collected after 1977 were primarily personal measurements (N=13 000) taken to represent full-shift exposures [8-hour time-weighted averages (TWA_{8h})] and covering about 300 jobs. Charcoal tubes and passive dosimeters, with analysis by gas chromatography, were the primary sampling and analytical methods. More than 90% of the measurements collected after 1977 identified the job, department, date, measure (TWA_{8h}, peak, or ceiling), sampling medium, and kind of measurement [personal or area (5000 area measurements in 4 companies)]. Use of respirators during the measurement, whether the sample was representative of "typical" conditions, and the activities occurring during the sampling were also identified for many of the measurements. The measurements available prior to 1977 were generally short-term area samples collected for purposes of evaluating engineering changes.

Acrylonitrile monitoring

In 1986, the study investigators monitored 10 jobs in each plant 3—4 times, totaling about 400 measurements. Seven companies conducted monitoring simultaneously using their own sampling and analytical protocols. This procedure provided the opportunity to examine company measurements with the study measurements to evaluate their comparability across different companies (Zey JN, Stewart PA, Hornung R, Herrick R, Mueller CA, McCammon C, et al. Evaluation of side-by-side pairs of acrylonitrile personal air samples collected using different sampling techniques, unpublished results). This examination was necessary to ensure that the different monitoring procedures used by the companies were comparable, a necessary criterion for the proper ranking of jobs by exposure level across companies. The 2 sets of data (ie, company and study) were comparable, and no adjustment was deemed necessary.

To assess the occurrence of respirable fibers in the acrylic fiber plants and their potential to confound any lung cancer and acrylonitrile association, air samples were taken in 1 company and analyzed by phase contrast microscopy and transmission electron microscopy. No respirable fibers were found. Some web-like and rod-like structures were present that were not in the respirable range [>20 µm in diameter and >1 inch (2.54 cm) in length]. Data provided by a second plant indicated similar findings.

Standardization of job titles and development of exposure groups

A total of 127 000 unique job title, department, plant combinations was abstracted. This number was reduced to about 3200 combinations by combining jobs where workers (i) spent approximately the same amount of time in the same acrylonitrile department, (2) had similar tasks over the long-term (eg, a year), (iii) had similar exposures to other chemicals, and (iv) were expected to have a similar exposure distribution to acrylonitrile. Jobs were combined when they had a different title but were actually the same job (eg, chemical and process engineer) or when few people held the job (N<5). In the latter case, the job was grouped with the closest job in that same department. Grouping occurred only within departments and did not extend across different departments or companies. To illustrate the standardization criteria, the reactor operator and the assistant reactor operator were not grouped because the former generally collected quality-control samples, whereas the latter did not. The foreman and supervisor were kept separate when they spent different amounts of time in the production units or performed different tasks; otherwise they were grouped. Mechanics remained separate from instrument men and from electricians because of differing tasks and other exposures.

Table 1. Maintenance jobs, engineers, quality-control workers, and research and development staff, by percentage of time spent in acrylonitrile areas.[a]

Percentage of time spent in acrylonitrile areas	Job, department, plant combinations	
	N	%
None	3898	39
<5	977	10
10-19	834	8
20-29	458	4
30-39	461	4
40-49	70	<1
50-59	776	7
60-79	30	<1
80-99	274	3
100	2366	22

[a] The amount of time workers with the same production job title spent in the acrylonitrile areas did not vary by person. For most jobs it was 100% of the time.

Special procedures were used for developing exposure estimates for maintenance and quality-control workers, engineers, and research and development staff because these workers may develop specialties and often perform their duties in different locations in the plant and these duties are not reflected in their job titles. For each plant, the names and work histories of 200—500 workers who held one of these jobs for at least 2 years were sent to the companies and unions to estimate how much time each person spent in departments making an acrylonitrile product. About 20% of the person-job combinations (a subject could have contributed several jobs) were entirely confined to acrylonitrile areas, and about 40% spent between <5% and 90% of their time in acrylonitrile areas (table 1). The remaining person-job combinations were not assigned to any area involved in making an acrylonitrile product. On the basis of the amount of time spent in acrylonitrile departments, an additional 494 new job titles were developed (eg, mechanic/0, 5, 30, 50 or 80%). Workers who were reviewed but could not be characterized or who held jobs for less than 2 years were assigned to the acrylonitrile departments according to the likely proportion of time spent in the departments by all workers in that job.

In 1 plant workers in 2 acrylonitrile units with the unspecified job title of "operator" performed different tasks that resulted in a substantial difference in exposure levels. More than 90% of these workers (N=229) were identified with specific tasks by at least 1 of 2 long-term workers. Fifty-six were known to both workers, and there was independent agreement on tasks for 50 of them.

The end result of the standardization procedures was to create about 3700 exposure groups with a distinct set of task characteristics and similar exposure distributions, allowing the members of each group to be homogeneous for all the exposure metrics evaluated (TWA_{8h}, level and frequency of peaks, level and frequency of dermal exposure, and other exposures).

Development of job-exposure profiles

A document control notebook, with 370 to 1000 pages per plant, was developed to retain all relevant exposure information in an organized fashion. To facilitate retrieval of crucial pieces of information during the estimation procedure, a software system was developed, called job-exposure profiles, that stored the relevant data (3). For each exposure group a profile was developed that identified information on the process flow, equipment, job location, tasks performed, changes that took place that were likely to have affected exposure levels in the job, production rates, unusual occurrences, overtime practices, frequency of acrylonitrile exposure, acrylonitrile peak and dermal exposures, reported adverse health effects, concentration of acrylonitrile in liquids coming into contact with the skin, use of personal protective equipment, level of physical activity, ranking of the jobs by exposure (as estimated by the interviewees), and other chemical exposures (yes; no). In addition, the page number in the document control notebook where the information was located was identified with each piece of data.

A level of confidence was assigned to each variable in the job-exposure profiles. High confidence indicated that the information was obtained from a paper copy of a company or union report. Moderately high confidence meant that the information came from 2 other sources: interviews, the study investigator's judgment, or company or union review. Moderate confidence indicated that there was only one other source of information. This term was generally assigned where the company or union review changed what had originally been entered by the industrial hygienist of the study. Low confidence indicated that the information was missing or contradictory or based entirely on the judgment of the industrial hygienists.

The information on the manufacturing process had the highest level of confidence; 83% of these data were either obtained from company paper records (high confidence) or confirmed by a second source (moderately high confidence) (table 2). Location, level of physical activity, and tasks were also generally well documented. Between 60% and 70% of the observations in these fields were found on company reports or confirmed by a second source. About 50—60% of the information on chemicals, dermal exposure, and peak frequency were confirmed by 2 sources.

Exposure estimation procedures

The primary goal of the study was to evaluate the relationship between exposure to acrylonitrile and various causes of deaths. To accomplish this objective, TWA_{8h} values of acrylonitrile exposure were estimated for each job, department, plant combination by time period. The time periods, the minimum duration of which was 1 year, were formed from the start and stop dates of the workplace changes that were documented in the job-exposure profiles to create periods when acrylonitrile exposures were expected to be homogeneous for any given job. The implementation of a workplace change that affected exposure levels determined the start of a new time period. Thus jobs in acrylonitrile departments usually had multiple time periods, whereas others, such as those in administration or in nonacrylonitrile departments, had a single time period because no changes occurred that affected exposures of the jobs in that department.

Several procedures were considered to develop the actual job, department, plant, and time-period exposure estimates. The procedure of choice was statistical modeling because it develops unbiased estimates (4). This method requires measurements before and after each important workplace change, however. Although the number of measurements for this study was substantial (N=18 000), no single plant, or groupings of companies, had data to apply a statistical approach to all time periods. The use of semiquantitative exposure categories (eg, low, medium, and high) with midpoints or semiquantitative descriptors was also considered, but was discarded because this approach did not make full use of the abundance of measurement data in the more recent years. The use of categorical rather than quantitative, estimates also results in a loss of power in a mortality analysis when a small number of categories is used (5). A tiered approach was therefore developed that determined which estimation procedure was used, based on the data available and the characteristics of the job. The hierarchy consisted of arithmetic means wherever possible, followed by a time-weighting approach that weighted estimates of acrylonitrile concentrations in different areas of the plant by time; a deterministic approach, in which already developed estimates were modified based on workplace changes; and, last, professional judgment. All the estimates were developed using a software program to facilitate the estimation process and increase the accuracy of the calculations (6).

The arithmetic mean was used as the primary exposure measure because it is the most appropriate measure when cumulative exposure is considered to be the toxicologic mechanism (7). Although it is not entirely clear which exposure measure is the most appropriate for studying acrylonitrile, we relied primarily on cumulative exposure (2). Arithmetic means (table 3) were used when 2 a priori criteria were met (8). First, only personal, breathing-zone

Table 2. Level of confidence in the exposure information of the job-exposure profiles.

Variable[a]	Fields by level of confidence			
	High (%)	Moderately high (%)	Moderate (%)	Low (%)
Process	11	72	9	9
Frequency of exposure	1	49	42	8
Chemicals	0	50	38	12
Dermal exposure	0	59	35	7
Location	2	63	26	10
Peak frequency	0	53	40	7
Significant changes	3	16	75	7
Level of physical activity	0	68	30	2
Tasks	3	60	24	13

[a] The variables "process" and "chemicals" were associated with departments, and each had 246 entries. The other variables were associated with the job, and each had 1978 entries.

Table 3. Estimates by method.

Method	N	%
Arithmetic means — full shift, ≥6 measurements, personal	437	4
Arithmetic means — <full shift, <6 measurements, or area	171	2
Time-weighted average — using measurements	2174	21
Time-weighted average — using other estimates	1508	14
Deterministic	2971	29
Professional judgment — zero exposure	2542	25
Other professional judgment estimates[a]	372	4
Unknown	149	1

[a] Other professional judgment estimates, for example, were rarely in a low-exposed area, downwind of an acrylonitrile area, assigned to a laboratory where acrylonitrile was handled, and so forth. See the text.

measurements taken for at least 6 hours were accepted for calculating the means to ensure that full-shift exposures were represented. Second, a minimum of 6 measurements was required to ensure minimum stability for the estimate. Measurements taken under unrepresentative conditions (eg, a spill) were weighted based on the frequency of occurrence, as estimated by plant personnel. For example, a measurement taken during a turnaround that occurred once a year for 2 weeks was given a weight of 0.04 (14/365 days) in the calculation of the mean.

The time-weighting method, based on an exposure zone approach (9), was used for jobs that were performed in at least 2 different locations of the plant where personal or area measurements had been collected or exposure estimates developed (N=3682) (8). This method involved multiplying the estimated exposure concentration at each location by the percentage of time spent in that location and summing across locations. Where acrylonitrile was present, the average of the measurement means (N=2174), or of the operators' exposure estimates in that location if measurements were unavailable (N=1508), was used. For locations where acrylonitrile was not present, 0.00 ppm was used. This approach was used principally for jobs such as supervisors, engineers, and maintenance workers. For example, a supervisor who worked 90% of his or her time in an office in an administrative building and 10% of his or her time in an acrylonitrile department was assigned 90% of the time at an exposure level of 0.00 ppm and 10% at the average exposure of the operators in that acrylonitrile department.

Calculation of means and the use of the time-weighted-average formula completed many cells in more recent years, but could not be used for earlier years where measurements were lacking. For these earlier years a deterministic approach was used that modified TWA_{8h} estimates based on changes that took place in the workplace (eg, engineering controls, process changes, and work practices). There were 413 such changes. Of these, 17% were due to the addition or shut down of a unit (eg, start-up of acrylonitrile monomer production in a plant that had been producing other nonacrylonitrile products prior to that time). The remaining 343 were changes in local exhaust ventilation, enclosures, the process, work practices affecting production, the laboratory, loading, and the environmental department (table 4). Forty-seven percent of these changes occurred after 1977, and 53% took place before 1978.

For each change an effect and size were estimated. The effect was a correction factor defined as the ratio of the level of emissions before the change to the level after the change. Size was the proportion of exposure for a particular job contributed by a particular source compared with the exposure contributed by all possible sources. A likely range of the effect and size was estimated for each change by a chemical engineer with experience in the chemical industry. His estimate was based on monitoring data (35% of the changes), published reports of process and equipment developments in the engineering literature (4%), a combination of interviews with long-term workers and experience (28%), the interviews only (20%), and judgment or the experience of the engineer (13%). To derive an estimate for the production jobs affected plus all other jobs, such as supervisors, maintenance workers and engineers, that would have been affected by a change, an already developed estimate was modified for an adjacent time period using the size of the source and the effect correction factor. (For the formula, see reference 8.) Almost 80% of the 2971 estimates derived from this method were <1 ppm.

In addition to the preceding calculation, the engineer also estimated the maximum and minimum size and effects for each change. Three sets of estimates were developed to describe the uncertainty of this method: the best estimate (usually the midpoint of the range of the effect the change had on exposures, as estimated by the engineer) and a maximum and a minimum estimate (based on the extremes of the engineer's estimated range). This procedure allowed a sensitivity analysis of the method.

For jobs for which estimates could not be based on arithmetic means, the time-weighting or the deterministic methods, professional judgment was used (N=2914). Of these, 2542 were estimated to have no exposure, and about a third of the remaining ones had exposure levels of <0.1 ppm. For only 83 the exposure was >1 ppm. The bases for the 372 estimates greater than 0.00 ppm were as follows: the means were based on short-term area or personal samples or full-shift samples of less than 6 measurements (N=171); the job was not assigned to an acrylonitrile-exposed area, but on rare occasions may have gotten into one and resulted in very low (<0.10 ppm) levels (N=18); the job was not assigned to an acrylonitrile-exposed area, but was downwind of one (N=115); the job did not require handling acrylonitrile but was assigned to a laboratory where acrylonitrile was used, so that the estimate was equal to 10% of the estimate of the technician who handled acrylonitrile in that laboratory (N=24); all

Table 4. Major types of changes and the estimates of their size and effects, by type of operation.

Type of control	Type of operation								
	Fiber			Monomer			Resin		
	Estimated effect[a]	Estimated size[b]	Number of changes[c]	Estimated effect[a]	Estimated size[b]	Number of changes[c]	Estimated effect[a]	Estimated size[b]	Number of changes[c]
Local exhaust ventilation									
For quality control collection	10—100	M	5	10—100	S-M	5	10—100	M	2
Installed or modified control room	1—2	M	3	1.1—5	S-M	2	1.1—5	M	4
Installed or modified other equipment	1—5	S-M	32	1.1—5	M	3	1—10	M	22
Enclosures									
Miscellaneous point sources	1.2—5	M	6	1.1—5	M	2	1.5—4	M	6
Closed sewers	1.5—5	S-M	2	2—5	S	2	2—5	S	1
Process change									
Strippers	10—100	M	6	1.4—4	M	1	10—100	M	3
Catalysts	.	.	.	0.5—2	M-L	5	.	.	.
Work practice									
Draining on floors	1.5—5	M-L	3	.	.	.	1—5	S	2
Filter modifications	1.1—10	M	3	.	.	.	1—20	S-M	4
Reactor entry for cleaning	1.5—100	S—M	4	.	.	.	1.5—100	S-M	8
Continuous air monitor	1.1—2	M	2	1.1—2	M	2	1.1—2	S-M	3
Decreased spills or plugs	1.1—5	M	4	1.1—1.1	S	1	1—3	M	4
Equipment									
Tightened seals	1.1—5	S-M	6	2—5	M	3	1.1—5	M	3
Vapors recovered	10—100	M	1	1.1—3	M	3	.	.	.
Laboratory									
Installed or modified laboratory hoods	10—100	L	3	10—100	L	9	1—100	M	3
Environmental									
Ponds	.	.	.	0.9—10	S-M	4	1.1—3	S	1
Incinerators	0.5—3	L	2	1.1—100	S-M	2	0.8—100	S-M	3
Tank car or truck, loading or unloading									
Closed dome	2—10	S	3	1.1—2	M	1	.	.	.
Loading arms	.	.	.	1.2—10	M	5	.	.	.

[a] Effect was a correction factor defined as the ratio of the level of emissions before the change to the level after the change. A range of effects is provided because the effect depended on the source being affected and its effectiveness as perceived by the workers.
[b] Proportion of exposure contributed by a particular source compared with the exposure contributed by all possible sources for a given job (S=1—10%; M=11—49% and L=>50% of the total exposure).
[c] Number of times that change occurred in the plants.

other jobs in the area to which the job was assigned had exposure estimates of <0.10 ppm and there was no information to indicate that this job was any different (N=55); the job was assigned to a laboratory where acrylonitrile was rarely used and only in minute quantities (N=30); the job was determined, after the job standardization process had been completed, to be similar to another job so that the same exposure was assigned (N=65); or a ratio of 2 jobs in 1 time period was applied to one of them in another time period (8) to estimate the other (N=45). (An estimate was counted multiple times.) For 6 jobs, the process was no longer in existence. It was assumed that less care was taken with regard to acrylonitrile emissions than in later periods because hydrogen cyanide, not acrylonitrile, was considered to be the critical exposure. For these jobs, the estimates were derived by increasing the estimates for jobs performing similar tasks in the newer process by 50%. Finally, odor, using 16 ppm as the odor threshold reference, was used as the basis for 14 estimates (10).

Table 5 displays the number of job cells and exposure years by exposure category. Exposure years is, for a given study subject, the sum of all days at a TWA_{8h} divided by 365.24 days/year; this sum is added up across all persons. Twenty-five percent of the job-department-plant-time-period cells and almost 50% of the exposure years were estimated to have a TWA_{8h} level of 0.00 ppm, 27% (20% of the exposure years) were for estimates greater than 0 but less than 0.1 ppm, and 31% (22% of the exposure years) were between 0.1 and 1.0 ppm. Only 6% were estimated to have exposure levels of 1.01—2.0 ppm, 8% were estimated to be 2.0—10.0 ppm, and less than 1% of the estimates were at levels of >10.0 ppm. None of the latter 3 categories had more than 6% of the exposure years. One percent of the jobs could not be estimated. Examples of jobs at various levels are shown in table 6. The highest TWA_{8h} production jobs were generally in the fiber operations. People in production jobs had higher exposures than mechanics, who had higher levels than quality-control workers. The exposure levels decreased substantially over the period of study, particularly in the late 1970s when the standard of the Occupational Safety and Health Administration was promulgated.

Table 5. Estimates by level of exposure.

Level (ppm)	Frequency N	Frequency %	Exposure years N	Exposure years %
0	2576	25	97041	48
>0—<0.1	2796	27	40711	20
0.1—1.0	3244	31	43520	22
1.01—2.0	593	6	6916	3
2.01—10.0	833	8	11113	6
>10.0	131	1	1556	1
Unknown	151	1	1063	1
Total	10324	100	201921	100

Table 6. Exposure estimates by job and decade.

	Decade 1952—1959 (ppm mean)	1960—1969 (ppm mean)	1970—1979 (ppm mean)	1980—1983 (ppm mean)
Highest job[a]				
Asstant reactor operator in plant 1 (fiber)	6.89	6.89	4.36	1.85
Monomer operator in plant 2 (monomer)	.	3.54	2.80	0.31
Monomer operator in plant 3 (monomer)	.	16.82	6.18	1.26
Wet tow operator in plant 4 (fiber)	20.82	15.38	9.13	0.80
Polymer operator and helper in plant 5 (fiber)	18.78	18.04	3.73	1.24
Monomer operator in plant 6[b] (monomer)	0.71	0.63	0.49	0.38
Production laborer in plant 7 (resin)	.	7.50	3.04	0.68
Monomer operator in plant 8 (monomer)	1.91	1.90	0.77	0.29
Maintenance mechanic				
Plant 1	2.05	2.05	1.74	0.53
Plant 2	.	0.91	0.10	0.01
Plant 3	.	8.17	2.07	0.58
Plant 4	4.37	3.77	2.70	0.67
Plant 5	7.72	6.44	1.50	0.36
Plant 6	0.02	0.03	0.04	0.05
Plant 7	0.36	1.57	0.09	0.05
Plant 8	1.52	1.52	0.18	0.37
Quality-control technician[c]				
Plant 1	2.24	2.03	1.58	0.93
Plant 2	.	0.14	0.13	0.07
Plant 3	.	3.57	2.07	0.81
Plant 4	0.23	0.25	0.24	0.22
Plant 5	1.49	1.35	0.88	0.20
Plant 6	0.05	0.42	0.36	0.18
Plant 7	0.17	0.16	0.13	0.10
Plant 8	0.06	0.07	0.08	0.10

[a] Type of plant in parentheses.

[b] Measurements in this plant in 1977—1983 indicated lower exposure levels in the monomer operations than in the other monomer plants, and few workplace changes had occurred in this area over the study period, suggesting lower historical exposure levels.

[c] This job was assigned to a laboratory located in a building separate from the production operations and therefore could not be correlated with the production exposures. There were few changes in the laboratories in plants 2, 4, 7 and 8, suggesting that exposure levels changed little.

Several exposure metrics were developed in addition to the TWA_{8h} estimates to provide the opportunity to investigate risks from disease mechanisms other than cumulative exposure. Peak exposures were defined as 15-minute excursions that averaged 20 ppm or greater. The frequency of peaks was estimated where the TWA_{8h} was high enough for a peak of 20 ppm to be mathematically possible [ie, a minimum TWA_{8h} of about 0.6 ppm (20 ppm · 15 min/480 min)], and when a task was performed that was likely to produce a peak (such as taking a process sample in an open jar). Estimates of actual airborne concentrations taking into account respirator use were also developed by modifying the TWA_{8h} estimate by a protection factor, depending on the type of respirator used (5 for half-mask, 10 for full-face, and 50 for supplied air). The protection factor was further modified by multiplying the estimate by 0.67 for suspected ineffective use (11). Estimates of the mass of acrylonitrile inhaled were developed by modifying the TWA_{8h} estimate by the average level of physical activity (low, moderate, or high) required to perform the job, the average respiration rate associated with that activity, and the average tidal volume (12). Finally, because acrylonitrile can be absorbed through the skin (13), a dermal score was developed by multiplying the percentage concentration of acrylonitrile in the liquid with the estimated frequency of dermal contact and dividing by 100.

Each of the exposure metrics was developed for each job, department, plant, time-period combination. Each study subject with the combination was assigned the values estimated for the combination. A confidence in the TWA_{8h} estimates was identified based on knowledge of the tasks, environmental conditions, and the reasonableness of the measurements in light of this information. Exposure to 340 substances other than acrylonitrile was assessed on a qualitative (yes;no) basis only. Among the exposures with more than 20 000 person-years were acetaldehyde, acetic acid, acetone, acetonitrile, ammonia, asbestos, benzene, carbon monoxide, nonspecified catalyst, caustic, dimethylacetamide, dyes, formaldehyde, hydrogen cyanide, hydrogen chloride, lubricants, methanol, methylene chloride, phenol, phthalic anhydride, styrene, sulfuric acid, toluene, vinyl acetate, and xylene.

Evaluation of the estimation procedures

To determine how well the estimation procedures compared with the actual monitoring data, a reliability study was undertaken for 2 of the estimation methods (ie, the time-weighting method and the deterministic method) (8). This effort was independent of the estimation process, and the estimates developed for comparison were not used in the epidemiologic study.

The time-weighting method was used when job tasks were performed in multiple locations within a plant. For the reliability study, all job-department-plant-time-period cells (N=32) were identified that had at least 1 full-shift personal measurement and that also had secondary exposure information, such as area measurements or estimates for the operators in the appropriate locations. The concentrations for each location, from the secondary exposure data, were weighted by the percentage of time spent in the location and summed across all locations. This procedure was carried out without knowledge of the full-shift measurements. The estimates were compared with the corresponding full-shift measurements. For the evaluation of the deterministic method, a mean was calculated from the measurements of the most recent time period for a given job-department-plant cell. Without knowledge of the earlier measurement means, the means from the most recent time period were modified using the size and effect estimates developed for the deterministic method. Estimates were derived back to 1977—1978 (the start of the personal measurements) and compared with the means of the measurements for the corresponding years for that cell.

The difference between each estimate and its corresponding mean (the reference value) was summed across all estimates developed for this evaluation study for the 2 estimation methods. The average bias was calculated by dividing the sum by the total number of estimates. Imprecision was the standard deviation of the mean bias. Accuracy was the square root of the sum of the square of the bias and of the imprecision. Relative statistics were found by dividing the statistic by the mean of the reference values. Spearman correlation statistics were used to determine how the reference values and the estimates ranked the jobs.

The estimates derived from the time-weighting average method averaged 24% lower than the means of the measurements, and they had a relative imprecision of 168% (table 7). (The closer to zero the relative statistics, the better the estimate.) The estimates derived from the deterministic method had a relative bias of 1%, but a relative imprecision of 236%. The correlation between the estimates and the measurement means was moderate and statistically significant (r=0.6) for both methods.

Quality-control procedures

Several quality-control procedures were implemented to ensure as accurate and reliable estimates as possible. A protocol providing a detailed description of the estimation procedures was developed by the investigators and reviewed by the Acrylonitrile Advisory Committee and by company and union personnel. It was also sent to over 30 other interested parties, including government and university experts. Comments were received from many of these groups, and many of them were incorporated as appropriate.

The Advisory Committee, composed of prominent epidemiologists and industrial hygienists, reviewed the study on an annual basis and provided guidance. The companies and unions were provided an opportunity to review and comment on numerous steps in the exposure assessment process. The site visit report for each plant was reviewed by a second study industrial hygienist and then sent to the companies and unions for comment. The lists of exposure groups and standardized job titles were also provided to the companies and unions. A study industrial hygienist visited several of the companies for 1 to 5 days during the job title standardization process to review these results carefully. This visit also provided another opportunity to collect additional information on plant operations and exposures. All of the job-exposure profiles were reviewed by a second industrial hygienist on the project and by company and union representatives. The companies and unions provided comments on about 5% of the data items (either correcting or supplementing them), most of the comments adjusted the date when personal protective equipment became available. All exposure estimates were reviewed by a second study industrial hygienist for consistency and relative ranking. For 5% of the exposure estimates the complete estimation process and documentation were reviewed in detail. In addition, 10% of the estimates based on measurement means, the time-weighting, and the deterministic methods were recalculated using a different software program to ensure that they were mathematically correct. The estimates and

Table 7. Reliability measures by estimation method.

Statistic	Estimation method	
	Time-weighting method	Deterministic method
Number	32	177
Mean of measurements (ppm)	0.62	1.34
Standard deviation of the differences (ppm)	0.02	0.25
Mean of the estimates (ppm)	0.47	1.33
Bias[a] (ppm)	-0.15	0.01
Relative bias[b] (%)	-24	1
Imprecision[c] (ppm)	1.03	3.17
Relative imprecision[b] (%)	166	236
Accuracy[d] (ppm)	1.04	3.17
Relative accuracy (%)	168	236
Spearman rank correlation coefficient	0.59	0.58

[a] The mean of the differences between the mean of the measurement and the mean of the estimates.
[b] Relative bias, relative imprecision, and relative accuracy are bias, imprecision, and accuracy, respectively, divided by the mean of the measurements.
[c] Standard deviatiion of the differences between the mean of the measurements and the mean of the estimates
[d] Square root of the sum of the square of the bias and the square of the imprecision.

the data regarding their derivation (ie, all the information used to develop the estimates) were sent to the companies and unions for comment. Meetings were held with worker and company representatives to discuss the overall patterns of the exposure estimates and receive comments and further relevant information. The study investigators made numerous telephone calls to labor and company representatives to resolve outstanding issues. Agreement was reached on all the estimates.

Discussion

This report provides a detailed description of how exposure estimates were developed for a study of workers exposed to acrylonitrile. Presentation of such detail is necessary to evaluate fully the strengths and weaknesses of any project using quantitative exposure assessments. Over 10 000 estimates were developed for 3662 job, department, plant combinations over a 30-year time period; of them about 25% were 0.00 ppm and 25% were based on measurement data directly. The amount of exposure information collected for the study was substantial. Over 300 pages per plant were assembled from the many site visits to the companies, without counting the company and union reviews. The entire estimation process took over 11 person-years of the time of the study investigators and the company and union representatives.

Each estimate was developed to the hundredth of a part per million. Undoubtedly, it is not possible to estimate historical exposures to this degree of precision, and jobs that differ only in the second decimal point should be considered as having equivalent exposures. We report them in this fashion, however, as they represent our best estimate. Some investigators recommend that an arbitrary numeric scale be employed in estimation efforts such as this. We believe there are sound arguments for using a ppm scale. First, it was how the monitoring data were provided to the study investigators. Second, developing ppm estimates forces researchers to scrutinize the exposure information more carefully than might occur when cruder estimates are developed. Therefore, this is a mechanism that encourages careful evaluations of the data. Third, the ppm units represent the scale that is most familiar to industrial hygienists. We see no advantage in developing a new scale that requires conversion of ppm measurements before they can be used. The lack of experience of industrial hygienists in evaluating exposures on the new scale would seem to be a limitation, not a benefit. Fourth, some type of exposure is needed to anchor the level of disease risk observed. Although identifying a disease risk with a point exposure estimate would be inappropriate (eg, 2 times the risk of lung cancer at 5.76 ppm), the magnitude of the point estimate provides useful information.

The comparison of estimates derived from the time-weighting and deterministic estimation methods with actual measurements provided us with an evaluation of the overall accuracy of the estimates. Both methods had a fairly low amount of bias (24% and 1%, respectively) but larger imprecision values (168% and 236%). This level of bias falls within the level of error accepted by the Occupational Safety and Health Administration for a monitoring method for acrylonitrile (14). The correlation between the estimates and actual measurements was about 0.6, which is good. It is comparable to or better than that found in a study in which industrial hygienists provided with a limited number of current methylene chloride and styrene measurements ranked the jobs they observed (15). The authors found a correlation of about 0.7 between the job rankings and a larger set of methylene chloride measurements and a low correlation of 0.2 between job rankings for styrene and additional styrene measurements. Thus a correlation of 0.6 between historical estimates and measurements appears to be in the vicinity of what can be expected for current evaluations.

There are several limitations to this examination of the estimates. First, the gold standard was measurement data collected by the companies in about 1977—1987. Using these data assumes that the means of the measurements are representative of the true average exposures. In several instances, however, the measurement means appeared to be of questionable validity, even after adjustment of the means for the frequency of unusual occurrences (16). A second limitation of this study is that the measurements were only collected as far back as 1977. Most of the measurements were less than 2 ppm, and it is possible that the differences between the estimates and the measurements could have been greater in early years, when the exposure levels were expected to be higher. There is no way to determine if this variation occurred, however, because measurements from that time period are unavailable. It is of some comfort that less than 10% of the estimates and exposure years were greater than 2 ppm.

Using the time-weighting method for jobs that require people to work in several areas of the plant has its limitations, but the lack of monitoring data for some jobs necessitated this approach. One concern about using this approach of deriving the exposures of management workers in the area from operators' exposures is that it may bias estimates upward. On further scrutiny, however, the direction and degree of bias are less clear. Any given job can be considered to have 2 types of exposure, the ambient air, which has both near and far field components, and the tasks being performed in the job. The purpose of using the operators' average exposure was to estimate an average ambient air concentration in the operating unit. If the measurements were taken during the performance of high-exposure tasks, such as collecting a quality-control sample or cleaning a filter without ventilation, inclusion of these tasks may well bias upward the overall estimate for the management jobs assessed by this method. This bias is offset, however, to some degree by the fact that many of the measurements incorporated 3 sources of exposure that are likely to be lower than the ambient concentration in the operating unit, for example, exposure during lunch breaks in unexposed areas, exposures of production operators while they are in low-concentration control rooms, and exposure of the control room operator, who spent most or all of the time in the control room. The last alone could substantially lower the average. For example, if the air concentration in the control room was 0.05 ppm and the average of the 4 production operators' exposure was 2.00 ppm, inclusion of the control room operator's exposure of 0.05 ppm would drop the operators' average by almost 20%. In fact, the reliability study found that the estimates derived from this method underestimated the measurements by 24%. It seems, therefore, that the time-weighting method can be used to develop estimates for persons who spend time in several areas of the plant.

The deterministic method also had it limitations. The method was based on the assumption that determinants of exposure, primarily changes in the workplace, could be identified and estimated. Failure to identify important changes would, of course, lower the accuracy of the estimates. For the changes identified, however, we attempted to estimate the effect on exposures as accurately as possible. Two components of changes in the workplace were evaluated, size and effect. Other studies have simply estimated effect, but, because there were often many sources of exposure in these workplaces, we attempted to improve the assessments by adding the size component to the process. It would have been preferable to have had monitoring data before and after each change. Some of the effect estimates were actually based on monitoring data from the companies in this study and some from reports in the literature. Most, however, were based on descriptions provided by the long-term workers and on the experience of the engineer who developed the estimates after review of the interview notes. We recognize that this method was likely to result in a misclassification of jobs. To describe some of the uncertainty around the estimates, we developed a best estimate, a minimum estimate (an estimate of the least amount of change likely from the base-line estimate), and a maximum estimate (the estimate of the largest change likely from the base-line estimate). It is somewhat reassuring that the epidemiologic analysis found that the 3 estimates yielded nearly identical exposure-response patterns (2). Despite the difficulty in assessing the effects of plant changes in exposure levels, we believe this approach improves the quality of the exposure estimates. This conclusion is based on the results of the reliability study and also on our belief that ignoring these changes would be worse.

Professional judgment was the least desirable of the estimation methods. Most of the estimates from this method were 0.00 ppm, however, based on the fact that acrylonitrile was not present in the physical location these estimates signified. Of the remaining estimates based on professional judgment, most were below 0.10 ppm because acrylonitrile was used in small amounts at infrequent intervals. There were 2 situations in which the estimates developed from professional judgment were high. One was a monomer operation that used an older process that was shut down prior to 1965. Measurements were unavailable and communication with several people in the field indicated that the process was no longer used anywhere in the world. For the jobs in this process, we increased the estimates of jobs in the newer process by 50% for the early years, in the belief that the newer process was likely to have used better equipment and had greater efficiency in making the monomer than the older process. The second situation was in 2 companies where, in the early years, odor was reported on a continuous basis in 1 area. No measurements were available, but descriptive information suggested high levels. Odor has been perceived between 1.2 and 22 ppm (10). We used 16 ppm as the odor threshold as the interviews indicated that exposures were not well controlled. Because of our mistrust of this level, however, we indicated that we were not confident in these estimates. These 2 situations (the older process and the use of odor) affected only 20 estimates.

The study has several unique components in its exposure assessment process. One was the emphasis on documentation. The derivation of each estimate was carefully documented. Retrieval of the original information was facilitated by computerized data bases. Thus one can quickly determine what measurements were included in the calculations of each mean, who was in the interview when the estimates of time for a particular job were reported, and what the basis was for an impact of engineering controls on exposures. Documentation and computerization also facilitated modeling and descriptive statistics such as those found in the tables of this report.

The large number of job, department, plant combinations (N=3662) requiring estimates was due to the approach taken in developing the exposure groups. Unless we were sure the jobs were similar we kept them distinct. This approach increased the number of estimates required, but it provided greater confidence in the homogeneity of the exposures within each group. To increase further the confidence that we were dealing with comparable exposure groupings, jobs normally heterogeneous in exposure (eg, mechanic work) were identified and the names of the people holding them were sent to the companies and union for an estimation of how much time each worker spent in acrylonitrile departments. This was a unique component of the study that should have reduced misclassification because we assumed that the estimates developed for the workers were better than those by job. Such an approach was not necessary for most production jobs in the study because the titles conveyed a distinct and unique set of task, location and time characteristics and all workers holding these jobs tended to perform the same tasks.

A report in these proceedings used the perception of odor to estimate exposure levels and compared the estimates with the ones reported here (17). The correlation between the 2 sets of estimates was found to be 0.6. Because no comparison was made with the measurement data, it is difficult to interpret this finding. For example, if the estimates made in that study were compared with the measurement data, the correlation could be much lower. It may be simply fortuitous that the correlation between our estimates and the actual measurements in our reliability study was also 0.6. The odor study noted a high repeatability of information obtained from workers. It is useful to know that, at least over 24 hours, there was strong agreement between the raters' 2 sets of evaluations, because investigators performing exposure assessment must rely upon workers' observations for some information.

There are no other monitoring studies of acrylonitrile exposure with which to compare the estimates developed in this study. Only 3 other epidemiologic studies estimated quantitative exposure levels (18—20), and it appears that the exposure levels are of approximately the same magnitude as those in our study.

Summary

This report describes the exposure assessment process in a study of acrylonitrile workers. Several unique aspects of this study include identifying the time spent in acrylonitrile units for workers in maintenance and other jobs that move throughout the plant; describing in detail how the estimates were developed; comparing monitoring data across companies; evaluating the estimation methods with existent monitoring data; and using extensive documentation and quality-control procedures. The methodology described can be used in other exposure assessment efforts in cohort studies.

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