Addresses alternative approaches, data source considerations, exposure metrics, quality assurance, and appropriate documentation for possible future retrospective exposure data needs.

LEADING RESOURCE

Guideline on Occupational Exposure RECONSTRUCTION

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Protecting Worker Health

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About this Document

AIHA guidelines are developed through a consensus process that involves review by internal AIHA technical committees and external review by outside experts. Through this process, AIHA brings together volunteers with varied backgrounds and viewpoints. The intent of this document is to provide practical guidance to the practicing OEHS professional. This guideline is not a standard.

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Guideline on Occupational Exposure Reconstruction

Chapter 1: Introduction

As a practicing industrial hygienist (IH), one may be called upon to assess a worker's past exposures for a variety of reasons. These might include:

- Occupational epidemiology studies — both morbidity and mortality studies
- Surveillance — both medical and hazard surveillance
- Health complaints/illness clusters
- Worker (both employee and contractor) compensation/toxic tort cases
- Risk assessment

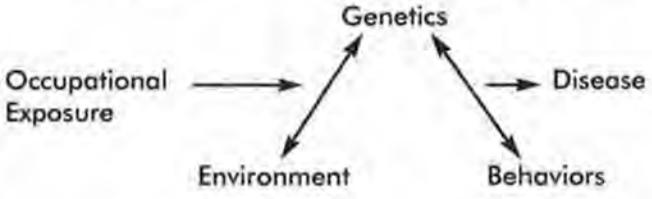
These situations require *retrospective exposure assessments*. This means they are conducted after the exposure has occurred, often after a disease or illness has been identified or reported. In the case of medical surveillance or risk assessment, this is after the opportunity to collect additional exposure measurements or establish baseline exposure levels have passed. In developing exposure assessments for these situations, the IH must rely on exposure and other data in existence. However, because much of the needed data is often missing, exposures must be reconstructed from existing data, historical facility information, interviews with workers, and professional judgment. This process is called *occupational exposure reconstruction*.

The purpose of an occupational exposure reconstruction is to determine the exposure scenarios where a worker or group of similar workers were exposed to specific stressors (chemicals, physical agents, or biological agents) of concern, the time period of each exposure scenario, and the frequency, duration, and intensity of each exposure. The typical approach used to reconstruct exposures is to link the work history of an individual worker or group of similar workers to each workplace exposure scenario over the time period(s) of interest. A major obstacle to conducting occupational epidemiology and other long-term studies is the assignment of exposure for each worker. Because of the retrospective nature, workers are typically not available for interview, as often they have moved to other jobs or locations, retired, or died. Thus, investigators must depend upon historical records to reconstruct exposures.

This guideline has been developed for two major purposes:

- The first is to present current good practices to the IH faced with the task of reconstructing or assisting with reconstruction of historical exposures. To fulfill this purpose, this document has been organized in a more or less step-wise fashion, starting with consideration of study design and scope, moving on to the actual exposure reconstruction activity, including the different exposure metrics, and ending with quality assurance activities and documentation. The document can be used to ensure that industrial hygienists have considered all major components in an exposure reconstruction effort. This document should help to organize and simplify what may seem to be a complex and overwhelming task.
- Secondly, this document may be used by industrial hygienists to help maintain and manage appropriate documentation for possible future retrospective exposure data needs.

Before beginning an exposure reconstruction process, the IH must first understand some basic concepts about the disease or injury process. *Epidemiology* is the study of the distribution of disease, broadly including diseases, illnesses, and injuries in humans and the associated causes and risk factors. To make the discussion flow more easily, the word *"disease"* will represent any adverse health outcome including mortality and injury. The primary assumption is that the exposure of interest is somehow related to the disease of interest. To illustrate how exposure is associated with or causes disease, a model is presented below. After the worker is exposed, three parts of the model influence the risk of acquiring the disease — other environmental factors, behaviors, and genetics.



- The first leg in the model is the environment, which includes occupational and environmental exposures other than the exposure of interest.

The environment also includes ambient atmospheric conditions, and workplace engineering controls. For example, a sheet metal worker who listens to heavy metal music and lives next to the airport will have less auditory recovery time, potentially increasing the effects of his or her occupational noise exposure. The IH will need to think of the causes, possible confounders, and risks for the disease as he/she reconstructs an exposure.

- The second leg in the model is behaviors, like smoking, sedentary lifestyles, alcohol consumption, use of personal protective equipment, and music listening. These behaviors may confound or obscure the true contribution that the exposure of interest makes to the risk for disease.
- The final leg in the model is the genetic make-up of the individual. This includes inherent susceptibilities or immunities to certain diseases, stature (ergonomics), and physical capabilities (stronger people get harsher jobs). While it is difficult to alter these factors, the IH needs to understand them when considering why some people get disease when exposed to levels much lower than others.

If the exposure reconstruction is being performed to conduct an epidemiology study or investigate an illness cluster, the IH will likely be working as a part of a team. Depending on the study type, an epidemiologist will likely take the lead, with industrial hygienists, physicians, occupational nurses, statisticians, and workers supporting the effort. Table 1.1 itemizes the processes in any study and the roles or activities that may be required by the industrial hygienist.

Table 1.1 — Industrial hygienist roles and activities by study stage

Study Stage	*Industrial Hygienist Roles and Activities*
Study Design and Startup	
General study design (see Chapter 2)	Assist with literature review: • Evaluate literature on exposure assessment for proposed design. • Evaluate past studies, if any, for similar populations and exposures. Support study design: • Discuss exposure assessment objectives and approach with others on team. What questions are to be answered by the study? • Clearly define the diseases(s), exposure agent(s) of interest, and the time period(s) of exposure. • Clearly define possible confounders and effect modifiers. What determinants are to be recorded during the exposure assessment work?
Feasibility verification	• Evaluate the scope of supporting information needed. • Investigate a sample of the broad types of records and information available, which includes any relevant monitoring data. • May require an initial site visit. • Determine and discuss the likelihood that available information is adequate to support the study exposure assessment objectives.
Study budget, timeline	• Develop resource estimates, time required, key deadlines, and budget for the exposure assessment. Consider personnel, equipment, laboratory analysis support, travel and expenses, as appropriate. Include the review processes, data handling procedures (e.g., data confidentiality), and preparation of final manuscripts/reports and publications.
Scope of reconstruction activity (see Chapter 3)	• Identify the investigation criteria that will be used in the reconstruction effort (e.g., in the case of medical surveillance, all workers who were exposed above an agent's exposure limit action level for at least 30 days in the prior calendar year.) • Identify the pool of individuals who may be impacted (i.e., the individuals who perform designated tasks or work activities within a given facility or areas of a facility where the agent of interest may have been used or produced), plus any workers in selected control areas (if a control group is included in the study design).
Exposure assessment protocols (see Chapter 4)	• Identify the procedures that will be used to apply the project criteria in consistent and objective manner. • Propose review and oversight mechanisms. Define expected reports, manuscripts. • Address IRB review comments, as appropriate. • Train personnel, as needed. • Plan for communication of study activities and findings to company, staff and/or trade union.

Table 1.1 — Industrial hygienist roles and activities by study stage (continued)

Study Stage	*Industrial Hygienist Roles and Activities*
Study Conduct	
Data search and assembly (see Chapter 5)	• Where data is sparse or limited to a few exposure groups, incorporate a comprehensive baseline survey, as possible. • Assemble, review, extract, and summarize records relevant to the exposure assessment for the study design, considering work histories, facility changes, exposures of concern and confounders, and other aspects. • Evaluate the information sources available to apply the project criteria. • Periodically review and communicate status with the project team. Include any issues or plan revisions in meeting either exposure assessment design goals or key deadlines.* • Conduct site visit as necessary to collect the information about the process or interview facility managers and workers. • Identify and contact any expert sources that you may need for advice or information (e.g., medical staff, engineers, other researchers.) *The IH may need to develop *ad hoc* solutions to missing information and other barriers. Review and comments by other team members or selected experts may also need to be sought.
Develop exposure estimates (see Chapters 6, 7)	• Select exposure metrics and group exposures. • Develop estimates for each worker or group of similar workers.
Perform data quality activities (see Chapter 8)	• "Validate" the exposure assessment to the extent possible and as stipulated in the protocol. • Provide input into uncertainty and sensitivity analyses.
Study Data Analysis and Reporting	
Data analyses, reports and manuscripts (see Chapter 9)	• Deliver the exposure assessments in a format useful for the planned analyses (per protocol and feasibility). • This may require various exposure metrics be generated. • Provide an accurate assessment of the exposure assessment assumptions, strengths, and limitations. • Support/prepare reports or publications.
Maintain documentation	• Document the exposure assessment and revisions, including any assumptions made during the exposure assessment.* • Document the QA/QC processes and procedures as planned in the protocol. • Provide sufficient details in files and reports for others to follow and verify the work, or to build on it in subsequent studies. *Appropriate documentation will aid in report writing, QA/QC auditing, and support for any future, follow-up studies.

Example Scenarios

To clarify the following discussion of the steps in exposure reconstruction, three example scenarios are introduced below and are referred to in this guideline. These include scenarios for reconstructing particulate exposures (Scenario 1 — Beryllium), vapor exposures (Scenario 2 — Trichloroethylene), and physical exposures (Scenario 3 — Noise). These examples illustrate real-world situations in which an IH may be required to reconstruct past exposures.

Example Scenario 1: Particulate Scenario — Beryllium

A Bicycle Company (ABC) buys several beryllium alloy tube products for use in constructing bicycle frames. The company has been in existence for 50 years, but has only used beryllium since 1982. Current employment is approximately 250. Past employment is not known.

The facility has two major work areas — frame manufacturing and bicycle assembly. Manufacturing tasks include shaping, grinding, threading, welding, and polishing the beryllium products. During welding and shaping, beryllium is heated. Facility maintenance tasks include: cleaning equipment (lathes,

grinders, pipe threader), surface cleaning (benches, floors), and disposal of spent material.

No personal protection has been used at ABC other than gloves (to protect hands from cuts and burns) and goggles and leather aprons (when welding). A new welding process was established in 1990, which reduced emissions. ABC has had an IH consultant sample for total dust exposures occasionally.

ABC wants to establish surveillance tools to identify trends in workers' exposure and indicators of workers' state of heath that are predictive of future disease. A morbidity study may be conducted to determine if an increased risk of illness is associated with exposure and if so, when did the exposure occur, at what exposure intensity, duration, and if there is a latency period between exposure and the onset of illness or disease. ABC has hired you as an industrial hygiene consultant to help with this effort.

Example Scenario 2: Vapor Scenario — Trichloroethylene (TCE)

You work in the environmental, health, and safety department of We-Fly airplane maintenance facility. The facility provides employee physical examinations. There appears to be a cluster of abnormal liver functions. TCE is a suspected cause. There are currently 125 employees, but there have been over 1,000 workers during the 35 years of operation.

At We-Fly, TCE is used to clean oily surfaces, remove coatings and paint, and clean brushes. We-Fly also recycles TCE. The TCE is sometimes sprayed and other times it is wiped or brushed on. Some TCE comes in drums, other times in small spray cans. Some applications are at elevated temperatures.

The facility is in a large open warehouse. Ventilation is limited to canopy hoods over the acid baths and some general ventilation during the summer when doors and windows are opened. Workers have been provided latex gloves throughout the plant's operation. Airborne TCE levels have seldom exceeded the TLV®.

In this exposure reconstruction, the exposure experience of each person with the liver abnormality, or common patterns in their work experience that would indicate the potential cause of their abnormality, could be developed. The abnormality could be associated with ongoing exposure or with upset conditions. The plan is to match individuals with the abnormality to individuals of the same gender and age without the abnormality. An exposure reconstruction is needed to determine the differences in exposure experience among workers that could explain the abnormality.

Example Scenario 3: Physical Agent Scenario — Noise

A small machine shop (M&P) makes custom parts for a variety of customers. There has been a number of hearing loss claims by M&P employees. The IH works for M&P's insurance company, who wants to know if the cases are work-related. The shop has been in operation for 30 years. There are 25 current employees with low turnover. The technology for stamping, milling, grinding, and polishing parts has not changed significantly over the years. The machines are all in one shop with no partitions. Employees rotate among machines.

Tasks at M&P include stamping and cutting sheet metal, grinding and polishing metal, and welding. Sources of noise include these tasks, as well as equipment motor noise. The shop area includes the operation of forklifts.

M&P started a hearing conservation program in 1985 that consisted of posting machines that were so loud people had to yell to be heard and placing circumaural muffs at each machine. Compliance was inconsistent during the early years. In 1995, you conducted an audit and designed a hearing conservation program including annual audiograms and sound level surveys with sound level meters and dosimeters.

In this case, the exposure reconstruction may be based on an exposure assessment of current equipment and conditions. It would also be important to know if work practices changed over time that could have impacted worker exposures. The assessment would then attempt to determine how much time individuals spent operating the various pieces of equipment and when they performed specific tasks. It would be important to know when in the past the workers performed this work.

Chapter 2: Consider Study Design

One of the most important parts of investigating the relationship between workplace exposure and occupational disease is selection of the appropriate study design. The best study design is one that has the most likely chance to answer the question of interest, or *hypothesis*. Depending on the question, the study population, and the exposure agent (chemical, physical or biological), broad study types may include an individual exposure or risk assessment (as in a workers' compensation claim), a hazard or medical surveillance program, or an epidemiology study. In cases where entire populations are of interest, epidemiology studies will likely be conducted.

Typically the epidemiologist or occupational physician will be responsible for selecting the study design. However, the industrial hygienist on the team may be asked to provide or interpret information about the facility, processes, or tasks to aid in defining the study population. The IH may also be asked to review available exposure data or production levels to assist in determining possible exposure categories and to consider other factors that may influence the final study design. This chapter highlights the features of the two primary epidemiology study designs used for occupational settings — cohort and case-control studies. Understanding the study types and their strengths and weaknesses will help the IH to better contribute to the study selection process.

Before embarking on a lengthy study, the team will usually conduct a literature review to see if this type of study has been done before on the population or agent of interest. Most peer-reviewed journal articles include recommendations to improve the study power, thus saving some time and problems in the study. The reader should review these articles to determine the approaches used and problems encountered in past exposure assessments.

Major Study Types

Cohort Studies

A *cohort study* is conducted when a population or group of individuals is followed over a period of time, either retrospectively or prospectively. Cohort study size can range from very large, national-level studies, like the British 1958 National Child Development Study, the U.S. Department of Defense Millennium Cohort, the Netherlands Maastricht Cohort Study, and the National Cancer Institute Agricultural Health Study, to those focused on an industry sector or special population, like the Nurses' Health Study I and II and the hexavalent chromium cohort study at Castle Hayne. In a cohort study, all study participants are presumed to be disease-free at the time exposure begins. Prior to conducting any case identification, the cohort is separated into groups of exposed and unexposed workers. By determining the groups prior to case identification, *selection bias* is minimized. One of the great strengths of cohort studies is the ability to explore different outcomes for a single or group of exposures or hazards using the same cohorts. The cohorts listed above have been used for years to investigate various outcomes ranging from breast cancer to lower back pain to psychosocial stress.

Generally, the exposed group is a special population within the cohort. For instance, the study could look at cancer among workers at a particular location (exposed), comparing their cancer experience with others that did not work there (unexposed). The exposed group can be further characterized by the level of exposure within the particular location as either a continuous, quantitative measure or a categorical measure (e.g., high, medium, and low exposure groups).

The unexposed group differs from the exposed group in that they did not have exposure to the agent of interest. The assumption here is that the only systematic difference between the two groups is their exposure. All other factors associated with the risk for disease are assumed to be randomly distributed, thus minimizing their effects. When these risk factors are not randomly distributed, they are a source of bias (bias is discussed later in this chapter).

The results of a cohort study can be generalized to populations that are similar to those that share the same characteristics as the study population. For example, in Example Scenario 2: Trichloroethylene (TCE), if the IH observes a positive association between job titles with a history of trichloroethylene use at We-Fly and renal cell carcinoma, he or she could generalize those findings to workers at other plants with similar demographics and exposure histories.

Cohort studies tend to be less expensive than other studies when they are conducted with existing

data from disease registries or plant medical records, though they can be very expensive when the amount of information to be collected increases beyond what is readily available. Cohort studies rarely involve personal interviews, but could include surveys that quickly add to the cost of a study. Some health researchers use cohort studies to generate hypotheses for further study using a case-control study design. The work environment described in Example Scenario 3: Noise lends itself to a cohort study. Hearing loss is not rare, the occupational exposure is limited to those that worked with the machines, and an unexposed population should be relatively easy to find. Obtaining information about genetics or behaviors is not necessary as long as the controls are selected from a similar population. Taking Example Scenario 3 a little further, if the exposed workers are mostly high school graduates that work in the industrial trades, a suitable control group might be engineering technicians or the administrative staff for the company. The control group should share any behaviors that are associated with the workers' socioeconomic groups, thus canceling out their contribution to the risk for hearing loss, and leaving the exposure to the machines as the primary risk. In this situation, it might be advisable to conduct a baseline noise survey to document the conditions near the end of the study period if exposure measurement data for the study are sparse. Obtaining current quantitative measures also assists in setting exposure groups more realistically instead of relying on somewhat arbitrary cut-points like the Action Level, and it could encourage the current workers and management to be more actively involved in the study.

Conversely, the findings of the cohort study has limited utility if the purpose of the study was to determine the risk of disease associated with a specific exposure because we have no information on other risk factors. This is particularly true for the unexposed and those without the disease of interest.

Cohort studies are also limited when the outcome is rare. To reach a level of reasonable significance, the size of the cohort may need to be very large (many people, years, or sites) to get enough cases (power) to actually conduct any meaningful analysis. (Study power is discussed later in this chapter.)

Some diseases take years to develop (the time between disease initiation to disease detection is called the *latency period*). Changing work conditions over the years make it difficult to generalize and apply study results to other populations. Because we rarely know when the disease process begins, we typically select the time the first exposure occurs as the beginning of the latency period.

Case-Control Studies

Case-control studies are always retrospective — the exposures always precede the health outcome or disease. A case is a person in the study who has been diagnosed with the disease of interest. A control is free of the disease of interest during the study period. The study is designed to determine the impact that certain factors, especially exposure to occupational agents, had on the risk for developing the outcome of interest for each study member. To get detailed exposure information for an entire cohort would be very time-consuming and expensive. A case-control study is smaller in scope, permitting more resources to go towards information gathering. Additionally, desirable information on environmental, *co-morbid risk factors*, behavioral, and genetic risk factors may be gathered.

Case-control studies are particularly useful when studying rare disease outcomes that would not be feasible to examine using a cohort study. All of the cases of the disease of interest identified in the cohort analysis can be used with select controls as needed. For example, chronic beryllium disease is rare and it may not be until 20 years after the first exposure to see the first cases. Because a case-control study uses available cases, cases may be able to be pooled from other locations or time periods if they share the same exposure of interest. In Example Scenario 1: Beryllium, the bicycle shop may only have 1 or 2 cases even if exposure to beryllium was significantly higher than the occupational exposure limit. By conducting a case control study using other bicycle manufacturers who use the same materials, more cases can be pooled to improve the study power. In national-level case-control studies, cases are obtained from disease registries and controls from other, comparable registers. The exposure reconstruction for these types of studies can be very complicated as detailed information about the occupational exposures for all study participants must be gathered and validated, usually from phone interviews or questionnaires.

The key to a good case-control study is selecting an appropriate control group. The better the selection, the fewer adjustments will need to be made to the study. An ideal control group for a study would be workers who share the same demographic profile, socioeconomic background and geographic conditions (i.e., drinking water, residential breathing air, food sources, etc.) but do not have the disease of interest. In addition, for cancer studies, researchers often compare the *case prevalence* to the general population, though that must be done cautiously because workers tend to be healthier than the general population.

The information and the process to gather information for cases and controls must be identical to avoid biasing the study towards one group. Thus in exposure reconstruction, the method that is developed must be applied equally to both groups. This can be accomplished by keeping the industrial hygienist or epidemiologist blind to the disease status of the study subjects to avoid differential collection and assessment of the data.

The ability to generalize study findings will be limited to people with similar exposures when compared to the control group. For Example Scenario 2, the study may desire to construct a dose-response relationship for exposure to trichloroethylene and renal cell carcinoma. Based on how the study was designed, the conclusions may be limited to only specific workers. For example, if the entire study population was over 50 years of age, then the study results may not apply to those younger than 50 years.

Study Design Issues

Study Power and Size

When a study is designed, its power should be adequate to detect an increased risk if it were truly present. This is basically controlled by the study sample size. Many studies fail to be conclusive because they lacked enough study participants for the effect to be observed to a significant degree. There are several factors to consider when doing a study size calculation:

- **Literature review.** During the planning stage, a literature review should be done to estimate the inherent risk in the unexposed population. This is then compared to the risk estimated in the exposed population. If the true difference between these groups is 3 times more risk for the exposed, the sample size can be much smaller than if there is only a 1.2 times more (i.e., only 20 percent more) risk in the exposed group.
- **Study power.** *Study power* is the probability that the study will detect a significant difference in risk at the level set in the study design. For example, if the IH wants to be 90 percent sure that the study will be able to detect a doubling of the risk for liver cancer in the exposed population when compared to unexposed population. The "90 percent" is the study power.
- **Case-to-control ratio.** In case-control studies, study power can be increased by increasing the *case-to-control ratio*, i.e., the number of controls per case. While electronic databases make matching cases and controls quite easy, there is a diminished return on power when the ratio is greater than 1:4.[1]

The size of a study refers to the number of subjects. Once the size of the study is determined (using the sample size calculations), there must be enough cases to analyze the impact of the study covariates (i.e., risk factors) on the outcome. The occupational physician or epidemiologist as part of the study protocol typically selects the study covariates. Study covariates must be determined during the design phase of the study and not after the data are collected and analyzed. Introducing new risk factors after the data are collected jeopardizes the integrity of the study as these data were collected to answer a specific question using a specific exposure-disease model. To continue with "Example Scenario 2: Trichloroethylene", the literature review reveals that impaired liver function was also associated with older age, tobacco use, alcohol use, and a sibling or parent with the disease (family history) in the general population. The study must be able to estimate how these other factors contribute to the overall risk. To obtain statistically stable results (a relatively narrow confidence interval), there will need to be enough cases (and controls) so that the distribution of these risk factors is sufficient to accommodate the analysis. A simple rule of thumb is 5–10 cases for each risk factor in the analysis.

There are many web sites that have online study power and sample size calculators with one comprehensive listed at: http://statpages.org/.

Bias

Bias is a type of systematic error that, when left unrecognized or uncontrolled, may cause incorrect interpretation of the study findings. Bias is best controlled during the study design phase. The most common types of bias are separated into two groups — bias associated with exposure and bias associated with the outcome.

Exposure Biases

- **Selection bias.** While case selection is based on the case illness or disease definition, the method used for selecting controls can introduce bias. Ideally, the controls should be chosen from the same population as the cases. This reduces some of the bias that can be introduced by behaviors and environmental exposures that may also contribute to the risk for disease. Using Example Scenario 2 for trichloroethylene and risk of liver cancer from workplace exposure in specific shop workers, unexposed office workers from the same plant might be selected as controls. Unbeknownst

to the study team, most of the office workers have been participating in a healthy lifestyle program for years, including smoking cessation and reduced alcohol consumption. Because the shop workers do not have the same health history as the office workers (i.e., the healthy lifestyle program), it would be difficult to separate the effects of alcohol and tobacco from the effects of the trichloroethylene on the risk for developing renal cell carcinoma.

- **Sampling (exposure measurement) bias.** As the industrial hygienist on the team, an individual will need to specifically consider the bias in the exposure measurements or *sampling bias*. When reconstructing exposure, the exposure in both cases and controls must be estimated. Many industrial hygiene samples are collected for a specific reason — compliance, worker complaints, union rules, and so on. These reasons will impact the usefulness and meaning of the sampling results in an exposure assessment. Regardless of the reason for sampling, workplace sampling does not routinely include unexposed or low exposed workers. The method used to estimate those exposures may be biased if they are based on samples from another location. Reviewing past industrial hygiene surveys and comparing sampling results across similar worksites within the industry may provide some basis for the sampling strategy and adjustment of exposure levels to reduce sampling bias. Using Example Scenario 3: Noise, the sound level surveys may have been conducted for compliance instead of characterizing exposure, and thus monitored the more exposed workers on more exposed days (worst-case monitoring). In reality, exposure intensities may have varied widely, and there may be workers in the group who routinely had lower exposure intensity.
- **Recall bias.** When interviewing the study subjects for exposure reconstruction, one may encounter *recall bias*. How a person remembers his or her past exposures and behaviors is influenced by his or her belief or knowledge that these exposures and behaviors are associated with a disease or adverse outcome. People with illnesses or diseases are more likely to report details about their past than people who are free from disease. There are several strategies for recognizing recall bias including comparisons of answers within and between groups of workers for consistency, asking questions about exposures for which there is actual data, and interviewing subjects more than once.
- **Information bias.** Simply, how information is collected and used to describe either exposure or a study outcome can introduce an *information bias* to a study. If the errors are independent of the outcome or exposure, then they will likely lower the ability of the study to detect the true risk. If the errors are not independent of either exposure or outcome, then the findings may be incorrectly increased or decreased. In the noise example scenario, all of the study participants were interviewed to determine their non-occupational sources of exposure to noise, including hobbies, power tool use, etc. But they weren't asked about MP3 player use. MP3 players are widely used across the population and any hearing loss attributable to them would be randomly distributed amongst cases and controls. The risk attributable to occupational noise sources would appear to be lower than the true risk because there would be some unaccounted, non-occupational hearing loss in the unexposed group.
- **Healthy worker effect.** When compared to the general population, people who survive in the workplace are generally healthier. Thus, interpretation of cohort studies that look at very special populations must be done with care. When reconstructing exposure, the IH should assist the epidemiologist to determine if and why some workers may have left that shop or industry earlier than others. Some workers may leave due to the fact that they become ill with the disease of interest, or they may leave because they are so highly exposed. It is important to use controls that have a similar longevity and similar industrial experience to the cases to reduce the bias introduced by the *Healthy Worker Effect*.[2]
- **Confounding from chemical mixtures.** A *confounder* is a factor that is associated with both the exposure and the study outcome.[2] While a study may be focused on a single chemical as the source of the risk for disease, the exposure may actually be a mixture of many chemicals or impurities that contribute significantly to the risk. In this case, the study exposure is a confounder as it is associated with the other chemicals in the mixture and also associated with the disease. When the risk is solely due to an impurity or unknown constituent of the mixture, the study chemical becomes a surrogate for the true exposure. It is also possible that the impurities may increase or decrease the study chemical toxic action.[3]

Outcome Biases

- **Confounders.** Age by itself is a risk factor for cancer. If the study is looking at liver cancer in trichloroethylene workers and cumulative exposure (exposure summed over a period of time) is used as the exposure variable, then the older study members will have more exposure. At the same time, just getting older increases their risk for liver cancer. Uncontrolled confounding can either falsely increase or decrease the observed risk. While controlling bias usually limits the ability to generalize the study results, it reduces the impact of the bias on the study findings. Matching the age of the controls with the age at which the case became a case reduces the confounding introduced by age. Other potential confounders include gender, smoking, ethnicity, and socio-economic status. If cases and controls are matched on too many variables, the control pool will need to be much larger to obtain a sufficient number of controls. When cases and controls are matched on a risk factor, the level of risk attributable to that factor cannot be measured. So, matching is usually only done when confounding is suspected. While there are statistical tests that can be done to identify confounders, the literature review will usually provide a list.
- **Effect modifiers.** An *effect modifier* is a risk factor that makes a study member more susceptible or protected from the effect of exposure on the outcome. It is unrelated to the risk of exposure and should not be confused with confounding. An example of an effect modifier is diabetes. Diabetics are more susceptible to the effects of air pollution than those without diabetes and diabetes does not cause air pollution or lung cancer. Some studies have shown the effect of noise on hearing is modified in those that smoke tobacco or use solvents. One way to identify effect modifiers in the analysis is to stratify on the suspected factor to see if the risk measure changes for both the exposed and unexposed groups. If a difference is observed in the stratified groups, then an effect modification may be involved. Those subjects with the effect modifier may be removed from the study or a separate analysis of this subgroup may be conducted.
- **Dealing with biases.** The best way to deal with bias is to spend some time carefully designing the study based on literature reviews, selecting an appropriate comparison group, matching cases and controls on potential confounders, collecting data independent of case and exposure status, testing the data for evidence of bias, controlling for confounding and effect modification, and ensuring that the interpretation of the results is within the limitations of the study design.

Level of Detail

For the purposes of using exposure information in an epidemiologic study, the level of detail is dictated by the quantity and quality of the data available to both the industrial hygienist and the epidemiologist. Detailed work histories, job titles, and locations can be used to adjust individual exposure assignments and improve the specificity of the exposure-to-outcome model. There are two schools of thought on the way to approach the level of detail during the analysis of exposure. One might start with dividing groups into exposed and unexposed and then increasing the number of levels in the exposed group to see if a dose-response relationship can be established. The other approach is to treat exposure as a continuous variable first and, if the results are not significant, collapse into exposure categories that can accommodate the number of exposed individuals. For example, if there are 10 cases, individuals may only be classified as "exposed" and "unexposed." If there are 30 cases, then exposure might be categorized as "Low," "Medium," and "High" provided that each category has at least 5 cases, preferably more. (See Chapters 3 and 6 for further discussion of exposure metrics.)

Chapter 3: Identify Scope of Reconstruction

Once the study design has been selected, the IH can begin the exposure reconstruction. The first step is to clearly identify the scope of the reconstruction. This step places limits on the reconstruction effort. It includes clarifying the goals of the reconstruction, and defining the population(s), time period(s), location(s), and stressor(s) of interest.

Goals of the Reconstruction

Exposure reconstruction can be undertaken for a variety of purposes that directly affect the methods used and the resources required, and thus the scope of the assessment must be clearly defined at the outset. One important starting point is a working definition of occupational exposure. A common theoretical construct used to define exposure is contact between a subject and a particular agent in the workplace. This theoretical construct is operationalized by assuming that contact occurs when a person spends time in a work environment in which the agent is present, resulting in at least some uptake of the agent into the body through one or more routes of exposure.

Biological monitoring for agents with long half-lives such as dioxins or cadmium can be used either to verify or assign exposure. However, biological monitoring is typically of limited value for reconstruction of exposures that occurred in the past, as often the biological levels have diminished by the time the assessment is taking place. There is also very little biological data available from historical records. The American Conference of Governmental Industrial Hygienists® (ACGIH®) has only 47 biological exposure indices (BEIs®) approved as of 2007. The availability of biological exposure data may change in the future as more biomarkers and valid biological monitoring is developed and utilized in exposure monitoring.

Exposure Metrics

The exposure reconstruction process ultimately results in one or more *exposure metrics* related to the exposure-to-outcome model. (See Chapter 6 for detailed discussion of exposure metrics.) Exposure metrics can be either ordinal or continuous values that summarize the available exposure information in a systematic manner, thereby providing a basis for making comparisons between subjects and classification into exposure levels. Typically, exposure can be assigned as if the value will be used as a continuous variable. Most occupational diseases and illnesses have a biological gradient. If a true dose-response exists, those with high exposure will have a higher risk than those with no or low exposure.

Possible exposure metrics include:

- Ever/Never Exposed — High, Medium, Low (other categorical metrics)
- Duration of Exposure — usually calculated; considers
  - Date of first exposure
  - Date of last exposure
  - Frequency (full-time, part-time, seasonal)
- Intensity or Average Exposure
- Lifetime Average Exposure (including unexposed jobs)
- Lifetime Cumulative Exposure (calculated from duration of exposure and intensity of exposure)
- Peak Exposure Levels
- Peak Exposure Frequency

Occupational exposure reconstruction can be either qualitative or quantitative. A qualitative assessment is conducted to determine whether a specific person or group of people was potentially exposed to one or more chemical, physical, or biological agents at work or work-related psychosocial stressors. A qualitative assessment would identify scenarios under which exposure would have been reasonably likely to occur, and then determine whether any of these scenarios are applicable to the subjects of interest. A definitive yes or no response is not always possible, and therefore, the results of a qualitative assessment can sometimes be expressed in terms of the "probability" of exposure on an ordinal scale, such as high, medium or low.

A quantitative assessment includes an estimation of the duration and intensity of the exposure that requires substantially more information compared with a qualitative assessment. In general, quantitative assessments require measurement data that are applicable to the exposure scenarios being assessed. Typical quantitative exposure metrics include cumulative average, cumulative peak, and number of

peaks or excursions over a period of time. Peaks are generally considered to be a relevant exposure measure for outcomes that are acute, eliminated quickly from the body, and in which the response in non-linear. Exposure to acid aerosols and irritant particulates seem to fit this model. Occupational cancer may be more related to "time since first exposure" than any other exposure estimate because time to develop the disease may be a better indicator of risk than cumulative exposure to the agent.[2] However, peak exposures can also play a significant role in chronic diseases as well.[3]

Exposure measurements for specific subjects are rarely if ever available, therefore, the usual strategy is to group the measurements by job title or job code, and use the average of the measurements as an estimate for all subjects with that particular job. However, the degree to which the measurement data can be applied to a particular job is ultimately a qualitative judgment, the basis of which should be documented.

The biggest problem with assigning study participants an exposure measure is that those with true exposures are sometimes grouped with those without exposure. This is inherent in grouping workers and job titles when assigning exposure, especially retrospectively. In most groups, there are workers that have higher exposure than others, yet they are all assigned the same exposure.

Target Population

The target population must be clearly specified when defining the scope of exposure reconstruction. The study population size can range from large cohorts with thousands of workers who are enrolled in an epidemiology study to evaluate the relationship between occupational exposure and disease, to the assessment of a single individual from one particular factory to determine whether a disease may be work-related. In epidemiology studies, a cohort is established and exposure information is collected. In an industry-based study in which a cohort is formed based on employment in a specific industry or set of factories, their occupational histories can often be obtained from personnel files. An industry-specific *job dictionary* containing a list of job titles is established, and the titles in the work history are matched with the standard titles in job dictionary. In addition, information on production processes and chemical inventories is often available.

In a population-based study, the subjects typically report employment in a range of industries and occupations. In this situation, standard occupational *coding* systems are often used such as the Standard Occupational Classification (SOC) Codes from the U.S. Department of Labor, the Standard Industrial Classifications (SIC) and the North American Industrial Classification from the Bureau of Census (NAICS) from the U.S. Department of Commerce.

Time Periods

The time period during which exposures are to be assessed is of critical importance. Estimates of lifetime cumulative exposure levels may include assessments for jobs held 40 or more years in the past for which little or no information is available. In other cases, the time period to be assessed can be restricted to specific periods of employment in a particular industry, or a time period with biological relevance to the disease outcome of interest. For diseases with long latency periods, such as cancer, the biologically relevant exposures may have occurred 20 years prior to the first clinical signs of disease, while for other health outcomes, such as adverse reproductive events, the relevant time period of exposure may be months or even days.

Location(s)/Facilities

Exposures can vary widely within a particular industry, and therefore the specific location or facilities at which the subjects worked can be important determinants of exposure. Thus, it is highly preferable to have the specific name of the factory or facility at which the exposure is being assessed, rather than the general industry or type of facility. Ideally, detailed information regarding the conditions within the specific facility at which the subject worked can be obtained. However, a more general approach is often required in which information collected from work environments that are qualitatively or quantitatively similar is used. In these situations, an objective assessment of the similarities between the work environment for which the information on exposure was obtained, and the work environment in which the subject was employed is required.

Stressor(s)/Potential Cause(s) of Illness or Disease Cluster

The particular stressors to be assessed must be clearly specified to define the scope of the exposure reconstruction. The stressors to be assessed can include not just the particular agent of interest, but also other agents to which the subjects may have been exposed that could potentially interact with the

agent of interest, or confound associations with a particular disease. For example, in assessing exposure to TCE, it may be important to also identify other chlorinated solvents to which subjects may have been exposed. The exposure of interest may also be present in various physical or chemical forms and in different solubility states. The same exposure can be present as a dust, fume, powder, liquid, or combined with other chemicals with different solubility characteristics within the body.

In situations where a *disease cluster* has occurred in a group of workers and the cause is unknown, it can be useful to attempt to identify an agent or set of agents to which the cases may have been exposed. Biological plausibility should be considered in suspect agent identification. Interviews can be conducted to obtain detailed information on their work environment, the timing and location of job tasks, and the materials and equipment used from which a list of possible factors can be compiled. Even though a specific etiologic agent may rarely be identified, this type of investigation can lead to the identification of preventive measures.

Chapter 4: Establish Data Collection Protocols

Before beginning any data collection for the exposure reconstruction, the study team should establish a set of study *data collection protocols*. The data collection protocols contain the objectives and specific procedures to be used in the collection process. The protocols provide a road-map to facilitate efforts to develop accurate, complete, concise, and objective information necessary to address the original purpose for the data collection. The protocols define the overall plan that is to be followed so that activities can be managed in workable components and the data collection is consistent over the entire collection process even when multiple assessors are involved. As is mentioned in the introduction of this guideline, the data collection process is limited by the exposure-related data that was developed and documented in the past, or at least can be reconstructed from currently available documentation or by individuals' knowledge of prior exposure scenarios.

Once it is decided that a study needs to be conducted, plant legal staff may be consulted to determine if there will be an Institutional Review Board (IRB) review of the protocol. An IRB is an independent organization (academic, government, or private) that reviews research proposals to ensure that the research has value, people are not being harmed by the study activity, and that the privacy of study members is protected. The type of IRB approval depends upon the types of records to be used in the study, the information to be collected, and the security plan to protect the data from unintentional release. While most academic and government institutions have their own IRBs, private companies may contract with a private IRB firm if they do not have access to one through their company.

Study Detail

All data collection efforts have practical limits including:

- Availability of records;
- Resources that have knowledge of the source data such as prior employees, technical representatives or management and supervision;
- The makeup and size of the investigative team; financial resources, and
- Timing.

The study detail is a balance that is dictated by the practical limitations of the study and the required information needed to meet the original purpose for the exposure reconstruction. It is likely that the team will depend on the industrial hygienist to help establish the level of detail for the exposure assessment portion of the study.

Objective Data Collection

The data collection process should be transparent with respect to the original purpose for the exposure reconstruction. Virtually anyone involved or potentially impacted by the exposure reconstruction can inadvertently introduce bias into the effort. This is true of the investigators who may hope to find some new relationship between exposure and adverse health outcome to a company that hopes that no harm to workers was incurred in the past. It can even be true of individuals who are asked to help develop exposure assessment information who, in trying to be helpful, may embellish information or the state of prior conditions. The key to collecting objective data is:

- The establishment of clearly defined procedures to identify and compile information and apply professional judgment;
- The development of forms or databases that facilitate data collection with a comparable level of detail and in a consistent manner;
- Employment of systems that reduce compilation and data entry errors;
- Blinding to assure a comparable effort for all records involved (e.g. cases and controls), and
- Validation programs which are capable of evaluating the performance of the entire collection process.

Quality Assurance/Quality Control

Quality assurance/quality control programs should be in place to maintain the integrity and reliability of the entire data collection process. In this discussion, quality assurance (QA) is defined as the system of activities that provide the beneficiary of the exposure assessment the assurance that data used as a basis

for a decision meets defined quality standards. Quality control (QC) is a system for ensuring the maintenance of proper standards used in exposure reconstruction including periodic random inspection of the exposure reconstruction process. Components of a QA/QC program may involve dual coders, dual data entry, validation studies, blinding and evaluation of professional judgment.

- Dual coders means that more than one person compile and analyze the same information which is then compared to assure consistency. The goal is that the exposure reconstruction should be independent of the individuals conducting the reconstruction.
- Dual data entry is used to minimize inadvertent data entry errors. All the data are recorded by each data entry person. Computer programs are then used to compare the dual entered data to identify inconsistencies. Any inconsistencies are resolved by reference to source documents or other resources. The premise with dual data entry is entry errors are likely random and there is a low probability that a random error will occur at the same point in the entry process. If data agrees, it is assumed to be correct, if the data does not agree, the disagreement is resolved.
- Validation studies are used to evaluate the various techniques used to estimate exposures. For example, if significant quantitative measurement data is available, a portion, such as 20% of the measurement data, is put aside and not used in the development of exposure predictive models. Once the models have been developed with 80% of the data, the 20% of the data held in reserve are used to assess the performance of the predictive models.
- Blinding is used in many studies to assure that the same level of rigor is used for all data no mater if affected individual has or do not have an adverse health outcome. One form of blinding is that the exposure reconstruction team completes the entire exposure reconstruction prior to any analysis of the potential of an adverse health outcome.
- Professional judgment is the application and appropriate use of knowledge gained from formal education, experience, experimentation, inference, and analogy. The capacity of an experienced professional to draw correct inferences from incomplete quantitative data, frequently on the basis of observations, analogy, and intuition has been demonstrated.[4] The ability to draw "correct inferences" implies that professional judgment can be measured. An example of how professional judgment can be measured is the case where an assessor is asked to review the impact, on worker exposure, of a series of changes in engineering controls implemented over time. If the assessor is unaware that the series of changes reviewed included some changes with quantitative data, their ability to correctly predict exposure in these cases could be used as an indication of how well they correctly predicted exposures when quantitative measurements are not available. An example of professional opinion is where an assessor states his belief if an operation is safe or unsafe. This statement is a function of the criteria an individual assessor uses to make a decision and the weight used on each criterion. Professional judgments between assessors should converse to some point with some level of variability where professional opinions may not converge.

Many times at the start of exposure reconstructions, sufficient information is not available to prepare a detailed protocol because the scope and quality of the data is not known or there is no information on the level of reconstruction will be practical considering available resources (documentation, financial and human), or the time frame in which the reconstruction must be completed. For example, with the case of a health complaint, some level of exposure reconstruction may be needed within a period of days to weeks and in an epidemiology study, the timing may be several years. Pilot studies are often conducted to obtain information on the quantity and quality of potential exposure related information available along with and the likely resources necessary to extract and compile the information and complete the exposure reconstruction. The results of the pilot study are then used to prepare the final exposure reconstruction protocol.

Chapter 5: Identify and Search Data Sources

Once the study design and protocols are established, the IH can begin collecting the data to be used in the exposure reconstruction. This section describes potential data or information that may be useful in exposure reconstruction and briefly discusses the data's use. While it may appear to be an overwhelming amount of data, not all of the information will be available or useful. The IH should however, consider all the topics presented herein before beginning the exposure reconstruction work.

The approach used in an exposure reconstruction is dependent on the original purpose of the study. Possibly, an exposure reconstruction is required for individuals who are included in the study group because they either have a specific health outcome such as lung cancer (case) or are matched demographically to a case with the specific health outcome (control). In this situation, the individuals included are clearly identified but the individual's work history and exposures experience may be highly uncertain and ill defined. If there is an opportunity to obtain information about work history experience via interview with the individuals or surrogates of the individual, an exposure questionnaire approach may be used. If the available work history information is even more limited, (the last job worked or the job designation is very general), it may only be possible to determine whether exposure took place or provide a probability that the individual was exposed. If the individual was exposed, obtain an estimate of the likely exposure intensity from peer reviewed literature or other publications such as NIOSH Criteria Documents.

Another possible direction relates to exposure reconstruction efforts in the case where agents, specific facilities, or sites are being investigated. In this case, the more classical approach[4] of workplace, workforce, and work practice characterization can be used to identify exposure groups or exposure scenarios. The intensity of exposure can be determined based on historical quantitative exposure measurements, or other approaches based on determinants of exposure, modeling techniques, or professional judgment. Classically, many studies used job classification or department, or a combination of the two as the surrogate of exposure. Unfortunately job classification and department designation are usually established for purposes unrelated to the workers' exposure potential. Individuals with the same job classification, or who work in the same department, may have a highly varied exposure. This variability leads to misclassification of exposure, which in nearly all cases reduces the likelihood that a study can identify an association or effectively quantify the strength of the association. It is usually possible to more clearly identify actual exposure if other information is taken into consideration.

Many case studies or investigations will require exposure reconstructions that utilize components of both approaches outlined above.

Before getting fully into searching and assembling records, some feasibility and scoping work may be prudent. This initial phase should involve collaboration with the epidemiology (or other) investigation team on the study design and fit of the exposure reconstruction to the study's data analysis plan. This initial investigation can help better define the scope of work needed to meet the exposure reconstruction design goals.

One of the early study design conditions involves the extent of the work history reconstructions. What time period is relevant? (If the disease latency is reliably known, this may be a consideration.) How detailed must the reconstruction be? The common level of completeness of personnel records or medical records or other relevant records for the specific study population may be the determining factor for the utility of these records in the overall study.

Data abstraction forms and checklists can be important tools to assure consistent gathering of information over time and over the range of persons, jobs and facilities covered in the study. These also help document the work and provide a basis for effective auditing of the data assembly and extraction processes.

Personnel records are often a prime source of information including hire date, prior-to-hire experience (industry? job?), positions held post hire, periods of significant absence, and dates of termination (other job, retirement, disability, reduction in force). Most organizations' human resources/personnel departments have the personnel records. The records retention and archiving practices need to be established early in the study, ideally as part of a

scoping and feasibility stage. Are records retained post retirements of an individual and if so, how long are the records retained? Where are the records kept? Are they in computer files that can be read with current hardware/software? Are the records microfilmed?

Recognize that the records primary purpose is to track employment, benefits, and compensation. Thus, job titles may change for compensation purposes (Operator trainee, Operator 1, Operator 2, Lead Operator) but have indeterminate relevance to changes in tasks performed and thus to exposure potential. Perhaps the records will specify the section of the operation where the individuals worked. Maintenance assignments are often amongst the most difficult to decipher because such craftsmen may be assigned to specific segments of the operation, or may work wherever their skills are needed and thus have quite variable exposure potential.

Gaps of information in the personnel records may be bridged, somewhat, by a variety of techniques, including read-across from more complete personnel records of other persons in the same job/department, or by interviews of long-service personnel who may recall either individuals or recall general trends and changes in assignments, tasks, and work methods. Retirees may be a key resource for such information, with structured interviews and group meetings/group interviews as sometimes useful in building a "consensus" of key facts.

Medical records may be useful supplements to personnel records in reconstructing work histories. Medical records may present biases in that not all workers receive routine medical evaluations, and records may be more extensive and complete for a few individuals and quite sparse for many others. Some organizations may include details about prior work exposures, and lifestyle factors such as smoking history, alcohol consumptions or pre-existing conditions. Recognize that medical records may be confidential information, and may require releases and informed consent for access and use. Any legal and human study ethical issues related to medical records should be reconciled in a study protocol. The same comments and questions as above for personnel records (computerized, archived, etc) may affect medical records too.

Individual training records may be useful in establishing workers' department and work assignments by time period and possibly the agents with which they worked. Because of the costs and time involved, training usually is not performed unless a worker actually works in a specific area. Unfortunately, the lack of an individuals' training record does not assure the investigator that the worker did not work in the area, because many training records have rather limited retention requirements.

Manufacturing records may provide essential data such as dates of construction, and the dates and nature of significant changes in the process equipment and process materials.

Facility descriptions can include text, blueprints, and photographs. Either a formal or informal facility "historian" may provide access, or a process/facility engineering group may have such records. As for all other record categories, the study goals must drive the effort and range of this investigation into facility changes.

Process history records may reside in a process engineering or general engineering section. Some blueprints will show dates of change, which can provide clues to key dates of process modifications. These may be checked with a timeline of general personnel record dates of change also, as there may be a tie to hiring and start dates with a new process, or ties to reductions in force for a process modification leading to staffing reductions. Capital equipment may be inventoried, with purchase, installation and maintenance records available.

Production records can give time trends of volumes for various time periods (possibly compiled daily, weekly, monthly, annually), and for some operations, exposures may be scaled with production. World events can also drive production levels at certain facilities, such as shipyard production rates increasing during times of war or manufactured housing production rates increasing following Hurricane Katrina.

Purchasing records, if retained for relevant periods, can give insights on the volumes, composition, and sources of raw materials and process additives, as well as equipment. The retention and file retrieval issues are a key factor in how informative this line of information can prove to be.

Organization charts, manpower planning and scheduling information can give information, possibly about assignment rotations, as well as the numbers of personnel in the operations.

In addition to company maintained records, union records may be an excellent source of work history records prior to, during and after the study subject was employed at the facility or facilities under study. The other jobs that an individual held can be sources of significant exposures especially among skilled labor, such as welders, electricians, etc. that will perform the same basic job duties regardless of employment.

Finally, in many cases, social security administration records can be used to establish time periods

that specific individuals worked at a site. These records are usually available for each quarter of a calendar year. It should be noted that these records usually do not indicate where an individual worked in a facility, but rather that they worked at the facility.

Following is the type of workplace, work force and work practice information that may be useful in an exposure reconstruction.

Workplace Characterization

The workplace characterization involves the reconstruction of the process history of the site, including any information and data that may be useful to estimate exposure either directly or as determinants of exposure. For workplace characterization, the types of information that may be important include:

- Physical layout of the site;
- Location of each process unit;
- Buildings within the process units;
- Description of the process;
- Description of the chemistry;
- Design and actual production rates;
- Operating conditions, and
- Points and quantity of emissions.

It is also important to note how the workplace characterization changed throughout the time period of interest. For example, a process may have been moved to a different facility or a substitution may have occurred, eliminating exposure of interest from a process and replacing it with a non-hazardous one.

Sources of this information may include the following:

- Facility map, blueprints, or photographs
- Written process description (including process chemistry, raw materials, major intermediates, catalysts, etc.)
- Effective dates associated with the processes such as unit startup and or termination, or dates of significant changes in the unit or process that could have modulated exposures
- Process flow diagrams
- Process and instrumentation diagrams (P&IDs)
- Types of equipment (containers, vessels, pumps, tanks, etc.) and the size of the equipment
- Process conditions (e.g. temperature, pressure)
- Engineering and/or process controls that could affect exposure potential
- Quality control and quality assurance records
- Auxiliary operations descriptions (e.g. maintenance, utilities, laboratory, wastewater treatment, etc.)
- List of stressors by process or area including the dates when the stressor(s) were used
- Composition of chemical stressors
- Raw materials, support materials and products delivery, storage or shipping procedures for the facility (rail car, tank truck, drums, containers, etc.)
- Location of effluent drains and ditches
- Production rates
- Quantity of raw materials or support materials (such as catalysts, solvents, etc.) used for each specific time period of interest
- Proximity to other processes that cause exposure to stressors not associated with the process
- Accidents (including fires, spills, leaks, failures in engineering controls such as ventilation, etc)
- Routine preventative maintenance or scheduled shutdowns of processes or equipment

Workforce Characterization

The workforce characterizations attempts to identify where individuals worked and how long they worked there. Additionally, the characterization considers specific tasks or activities performed, the frequency and duration of these tasks. The goal is to identify, for each individual, all the possible exposure scenarios worked over the study period of interest. Sources of information pertinent to specific individuals or groups of individuals include the following:

- Personnel records
- Organization charts
- List of job titles
- Job descriptions
- Job assignments
- Task descriptions
- Shift Schedules
- Job/task rotation schedule
- Worker rosters (i.e. company, union) over time by classifications such as craft, job code, process area, department, union roster, etc.
- Training records that could indicate the types of jobs or tasks specific workers were qualified to perform
- Payroll records
- Human resource records
- Social security records (identify the years an individuals is employed at a site)
- Interviews with worker or family surrogate

Some of the workplace and workforce categories may be redundant, but sometimes the choice of words and examples given can help trigger recollection and guide the investigators to the right persons and segments of the organization. Records of these

may be found by talking to long-service production supervisors/managers, human resources/training departments, via long service lead personnel, and if relevant, in union agreements and union records.

Work Practice Characterization

The work practice characterization is the interface between the workplace and work force characterization. This characterization includes how tasks or activities were to be performed, order of the activities, and the requirements associated with each activity.

If written policies and procedures for work practices exist, they are typically only a starting point for insights into actual day-to-day work practices. Often, the practices are written for the way the work should be done, for health, safety, quality, and other reasons. The practices may or may not align with convenient and efficient ways to minimize the effort and time required to "get the job done." The same may be said about training materials. Thus, an honest appraisal by workers who were there on a day-to-day basis may be needed to confirm or modify the written records. Sources of this information may include the following:

- Operating procedures
- Preventive maintenance procedures
- Housekeeping procedures (e.g. how often and how was an area or equipment cleaned?)
- Emergency procedures
- Records of the content of training programs
- Formulation or product recipes
- In batch processes, equipment used and equipment configurations and operating conditions
- Use of personal protective equipment

Respirator and other PPE use is often difficult to accurately assess, especially in circumstances where person to person variability in adherence may be a factor. Might the irritant or other discomfort aspects of exposure have "enforced" the equipment use? Was the need for PPE only for certain infrequent and closely supervised activities, such as tank cleanout or major repair operations? Was PPE required or only recommended? Discomfort, especially for prolonged use in hot and humid conditions may be an indicator that due to human nature, rigorous adherence may have had some exceptions.

Exposure Measurements

Exposure measurement characterization is used to establish the intensity of exposure and possible exposure patterns, such as peak exposure, full shift exposure, or task-based exposure. It is highly unlikely that sufficient quantitative exposure measurements will be available for every exposure scenario. The existing exposure measurements are used to calibrate or validate determinants of exposure or models that are, in turn, used to estimate exposure for each of the exposure scenarios. In some cases, calibration or validation is not possible, and the exposure estimates are based on available literature or publications.

- Quantitative exposure measurements along with all the descriptive information associated with the measurement
- Assumptions and documentation associated with developing exposure estimates based on determinants of exposure such as level of control, frequency and duration of tasks, vapor hazard index, volatility, process conditions, etc.
- Assumptions and documentation associated with modeling including ventilation rates, location of sources, emission rates, exchange rates, exposure sinks, etc.

Quantitative exposure records are valuable information resources, particularly if extensive, long-term over the course of the study relevant time periods, and if part of a documented exposure assessment strategy. Understanding the data collection strategy, and the circumstances for the samples are fundamentally important. Were the samples from normal operation? Were they targeted to investigate specific circumstances, such as the most exposed conditions and tasks? Were they randomly collected over time and thus represent a good composite to estimate average exposure and the ranges of exposures? If not randomized, were the samples at least targeted to representative conditions? The answers to these questions will largely determine how the data may be used. It is very important to understand the sample types, meaning full shift, short term, peak, task, upset, investigative, etc.

When dealing with personal samples, occasional samples for random individuals can be informative, but ideally, a program will give repetitive measurements over time for different individuals in the group, and allow estimation of the intra- and inter-individual variability. This can help define the range of exposure for the individuals in the group, and the legitimacy of grouping the data for an overall average.

Area samples may likely represent investigations for specific tasks and specific activities, for upper-end exposures, or for routine exposure potential. The distinction is important. Also, the duration and frequency of personnel in the area or performing

the tasks must be understood to estimate time-weighted shift exposure, as well as to estimate long-term average exposure.

Sampling and analytical methods may have changed over time, and the impact of the changes may be considerable. Thus, it is important to establish the validity, specificity, sensitivity, and accuracy of each of the sampling and analytical approaches used. Instrument calibration records are part of this, as is knowledge of laboratory proficiency as established by QA/QC reviews and proficiency analytical testing (PAT) round robin testing results.

The limit of detection (LOD) can change over time due to improvements in analytical methods. For example, the LOD for an analytical method could have decreased from 5 milligrams per cubic meter (mg/m^3) to 0.5 micrograms per cubic meter (mg/m^3) over the study period. Therefore, non-detect samples (samples that have no detectable amount of the analyte on the sample) for the early portion of the study may be given a quantitative exposure assessment value in later years simply due to improvements in sampling and chemical analysis technology. Data at or below the LOD is referred to as censored data.

Several different approaches have been proposed in the literature regarding how to incorporate censored data into the interpretation of quantitative data. Depending on the data set, you may find it simple to try the different LOD replacement values to determine whether the resulting differences really matter. More discussion of the techniques available to interpret LOD data can be found in Attachment A (Finkelstein 2001, Hornung 1990, Anonymous 1994).

Chapter 6: Select Exposure Metrics and Group Exposures

In occupational epidemiology an exposure metric is a variable that characterizes (quantitatively or qualitatively) one or more exposures of interest. Exposure metrics can be either ordinal or continuous values that summarize the available exposure information in a systematic manner, thereby providing a basis for making comparisons between subjects and classification into exposure levels. The selection of the type of exposure metric utilized in an exposure assessment is directly dependant upon the type and amount of information available for that exposure. The greater the amount and level of detail available, the more defined the exposure metric. Conversely, the lesser the amount and level of detail available, the less defined the exposure metric.

In this chapter, a number of different types of exposure metrics that are used in reconstructing occupational exposure for epidemiological studies will be discussed. This includes litigation, worker's compensation, and other reasons to reconstruct exposures. Exposure metrics range from relatively simple qualitative dichotomous variables, such as a "Yes/No" approach to exposures, to relatively complex quantitative variables, such as cumulative exposures. There are a number of different exposure metrics, multiple approaches to defining these metrics, and variations of exposure metrics are constantly being introduced into the literature through innovative methods. The trichloroethylene (TCE) scenario will be loosely used for the examples in this chapter.

Checkoway describes a hierarchy of types of exposure data that can be used to create exposure metrics, which in turn describes the hierarchy of desirable exposure metrics.[2] The hierarchy of broad exposure metrics ranges from the best metric of quantitative metrics to semi-quantitative metrics to qualitative metrics. Within these broad categories are a number of different methods that are used to create a wide variety of exposure metrics.

The best exposure metric is based upon quantified exposure measurements, normally from traditional industrial hygiene monitoring, for each worker. Each worker would have valid quantitative exposure data for the time period of interest with little to no gaps (time periods where no exposure data exists). While this is the best exposure metric, it is normally only the case for an individual worker or a very small group of workers. It is rarely available for large cohorts that can easily number into the thousands. Even the most complete quantitative exposure records for these large cohorts will still have large gaps in data that can be completed by various methods which are discussed in more detail in Chapters 7 and 8.

A quantitative assessment includes an estimation of the duration and intensity of the exposure that requires substantially more information compared with a qualitative assessment. In general, quantitative assessments require measurement data that is applicable to the exposure scenarios being assessed. Exposure measurements for specific subjects are rarely, if ever, available. Therefore, the usual strategy is to group the measurements by job title or job code, and use the average of the measurements as an estimate for all subjects with that particular job. The process of grouping similar job titles together is often referred to as "collapsing job titles" or creating groups of similarly exposed workers. An example of a job title collapse is shown in Figure 6.1 that illustrates a group of job titles with similar job tasks being collapsed into two general job title groups. However, the degree to which the measurement data can be applied to a particular job is ultimately a qualitative judgment, the basis of which should be documented.

The next best source of exposure data is at the job or task level. Again, this information normally comes from industrial hygiene monitoring of a group of workers performing the same job or tasks. Only a small number of workers or shifts have available exposure data with not all workers represented. The monitoring information is then pooled together to create an exposure pattern that can be applied to all workers associated with that job or task. A substantial amount of exposure data is needed to complete this type of exposure metric as multiple data points are needed for groups of jobs throughout the years encompassed in the study period.

When only a limited amount of exposure data is available, a semi-quantitative exposure metric may determine exposures better than qualitative metrics. A semi-quantitative assessment is an estimation of duration and intensity of exposure that is based upon a moderate amount of information, but not enough to establish a quantitative exposure assessment.

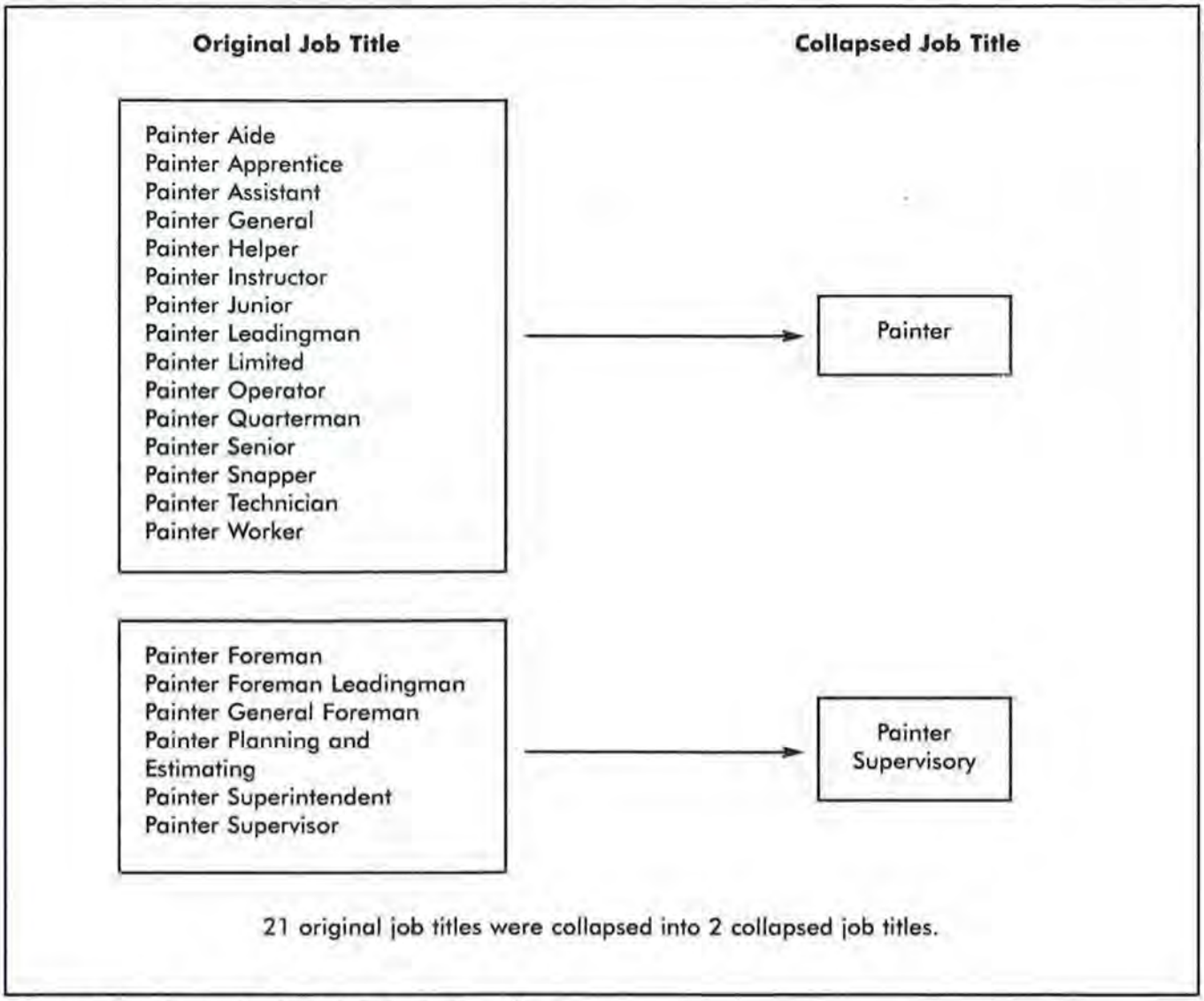


Figure 6.1 — Example of a Job Title Collapse[5]

For example, industrial hygiene monitoring data may be available for a limited number of years or jobs that provide insight into exposure patterns, but not enough to establish a quantitative metric for the entire study population. Semi-quantitative exposure metrics are often given categorical assignments in the epidemiological analysis that can separate between highly, moderately, low, and not exposed groups based on some exposure data. For example, you may have enough information to group exposures on a scale such as not exposed, < 0.1 x the OEL, 0.1 to 1 x OEL, or > OEL. Then, it may be possible to say more about exposures than with solely qualitative (e.g., no, low, medium, high) exposure metrics in situations where you do not have sufficient data to complete a full quantitative exposure assessment. There are some design issues in properly constructing dose estimates from semi-quantitative scale assessments, either with equally on non-equally spaced categories. However, it is more likely these issues will fall in the realm of the epidemiology analyses than in the conduct of the exposure assessment.

Qualitative exposure metrics do not need exposure data and are generally assigned by the exposure assessor or the exposure assessment team. While still very valuable in many epidemiological studies, qualitative exposure metrics do not provide the level of information (such as dose/response relationships or comparison to OELs) as quantitative or semi-quantitative metrics.

A qualitative assessment is conducted to determine whether a specific person or group of people was potentially exposed to one or more chemical, physical, or biological agents at work or work-relat-

ed psychosocial stressors. This determination of exposure can either be time-specific (i.e. by year, five-year, or decade) or can be determined for the entire period of the study.

A qualitative assessment would identify scenarios under which exposure would have been reasonably likely to occur, and then determine whether any of these scenarios are applicable to the subjects of interest. A definitive yes or no response is not always possible. Therefore, the results of a qualitative assessment can sometimes be expressed in terms of the "probability" of exposure on an ordinal scale, such as high, medium or low. The yes/no or ever/never assignment can also be given a confidence level such as high, medium, or low in another method to estimate the likelihood of exposure.

Qualitative exposure metrics can range from dichotomous categorizations, i.e. Yes/No or Ever/Never, to various durations of employment or rankings of jobs/tasks based upon potential for exposure. Duration of employment is based upon work history information and is based upon the number of days or years a worker spent in a job that had a potential for exposure. Kubale et al. used duration of employment to assess a confounding exposure when no exposure assessment data was available for a study examining the relationship between leukemia and ionizing radiation.[6]

Exposure Metrics

The exposure reconstruction process ultimately results in one or more exposure metrics. These metrics can be applied to the main exposure of concern, potential confounders, and/or effect modifiers.

Possible Exposure Metrics include:

- Ever/Never Exposed
  - Yes/No
  - High, Medium, Low, None
  - Ever employed in an exposed job
  - Ever employed in the industry
- Job or Task Rankings
  - Highest potential for exposure to lowest
- Duration of Exposure
  - Length of Employment in an exposed job or task
    - Days or Years Exposed
- Intensity or Average Exposure
  - Time Weighted Averages
  - Average radiation exposure
  - Average decibel level
  - Tasked-based averages
  - Frequency (full time, part time, seasonal)
- Lifetime Average Exposure (including unexposed jobs)
  - Average parts per million (ppm)
  - Average milligrams per cubic meter (mg/m^3)
- Lifetime Cumulative Exposure (Duration x Intensity)
  - Total Years in an Exposed Job (Person Years Exposed)
  - Cumulative Exposure/Years (PPM-years or mg/m^3–years)
  - Duration of exposure above a specified intensity (i.e. Years above 0.5 OEL)
- Peak Exposure Levels
  - Highest average exposed job
  - Highest exposure ever received
- Peak Exposure Frequency
  - Peak exposure per day, week, or year
- Internal exposure (received or retained dose)
- Confidence Ratings (High, Medium, Low)

Ever Exposed, Never Exposed

This dichotomous exposure metric is one of the most basic exposure metrics applied in reconstructing occupational exposures. This metric simply determines if a worker or job title was "ever" exposed to a chemical/physical/biological agent or other exposure of concern. This method is commonly used when there is no exposure data available, and is most often used in establish whether an occupation relationship exists between a hazard and a health outcome.

The first step in applying this method is to define "ever." Most exposure assessors will define "ever" as having a significant likelihood to have been working with the exposure of concern or working nearby the exposure of concern for some set period of time such as once per week or once per month. If the worker would have handled, worked with, been in the vicinity of, or any other number of factors the worker or job title would receive a positive score (normally Yes) for the exposure of concern. If the worker's job title or tasks indicate that they would have not been exposed to the exposure of concern, then they would receive a negative score (normally No). Ever can also be defined as a fraction or percentage of an occupational exposure level, i.e. above 10% of the OEL would be classified as "ever" and below 10% of the OEL would be classified as "never." For some exposures, the range between low occupational exposure and non-occupational exposure (hobbies, consumer products, and environmental media) can begin to blur and will require criteria for decisions to be consistent. Table 6.1 illustrates an example of this type of metric.

Table 6.1 — Ever/Never Exposure Metric for Exposure to TCE

Job Title	*Ever Exposed*
Secretary	NO
Automotive Mechanic	YES
Rubber Worker	YES
Accountant	NO

Ever/never exposed designs do not give data for quantitative risk assessment, and do not help define a dose-response relationship, which limits the utility for setting quantitative risk-based limits. A simple combination with the years in the possibly exposed jobs gives the metric duration exposed or person years at risk, which is explained in greater detail later in this chapter.

Some studies have added a "probability" of exposure with the ever exposed, never exposed design. In some of the studies, the probability was based on an assessment of the prevalence of exposure of personnel in an industry. The National Institute for Occupational Safety and Health's (NIOSH) National Occupational Exposure Survey has been used to set the exposure prevalence.[7] Probability for a group can give substantial exposure misclassification, because the prevalence for a group may not represent an individual accurately. Subjective probability scores assigned by expert opinion might also be used with an ever/never exposed design. The probability rating scale should be defined in advance with the investigative lead team. Criteria should be clear to help guide consistent application. Such probability ratings can be used in sensitivity analyses where the outcome associations are checked by first including all subjects, then selectively dropping out those with lower probability scores, to see if the results remain or attenuate.

Job or Task Rankings

The ranking of job titles or job tasks can also provide insight into the relationship between an occupational exposure and a health outcome. Rankings are often used to give an order in categorical analysis. The rankings can be divided into tertiles or quartiles with the highest rankings jobs in the highly exposed category and progressing downward (i.e. Highest exposure (1), medium exposure (2), low exposure (3), etc). However, it is also limited by not providing quantitative risk assessment in order to define a dose-response relationship. Rankings are best used with very limited or no exposure data available.

The exposure assessor is provided with a list of unique job titles or job tasks and can either collapse similarly exposed groups to reduce the number of titles or work directly with the unique titles. The rankings are assigned directly to the titles with titles being ranked in order of their estimated exposure. Table 6.2 illustrates an example of a simple job rankings exposure metric.

Table 6.2 — Job Title Ranking Exposure Metric for Exposure to TCE

Job Title	*Ranking*
Secretary	4
Automotive Mechanic	2
Rubber Worker	1
Accountant	3

Duration of Exposure

Duration of exposure characterizes exposure based upon the amount of time that a worker was employed in a job that was potentially exposed to the exposure of concern. This metric can range from simply knowing if the worker was ever employed in the industry to dates of first or last exposure to person years at risk. Duration of exposure is beneficial when work histories are available but exposure data is limited or non-existent, and should be used when the work histories collected are reliable and complete.

Determining if a worker was ever employed in an industry is a basic metric of duration of employment. However, it only adds a small amount of information to the overall picture. Being ever employed in an industry is only used when exposure data is not available and work history information is very poor.

Dates of first and last exposure are metrics that are used when determining whether the latency period of the health outcome is of concern. The latency period of a health outcome is the time from exposure to the first symptoms of the disease. Knowing the first or last dates of exposure can help determine the latency period of a health outcome if it is not already known.

The frequency of exposure is the number of times an exposure occurs for a determined amount of time. Some exposures may only happen annually or monthly, such as certain types of maintenance procedures. These types of exposures can add significantly to overall exposure pattern, and it is important to quantify the frequency of their occurrences. Quantification of frequency can include daily, biweekly, monthly, quarterly, or annually.

Table 6.3 — Example of an Ever/Never Exposure Assessment

	1972	*1973*	*1974*	*1975*	*1976*	*1977*
Job A	YES	NO	NO	NO	NO	NO
Job B	YES	YES	YES	YES	YES	YES
Job C	YES	YES	YES	NO	NO	NO

Length of employment in an exposed job is an excellent metric of duration of employment. This metric allows for the separation of time spent within an exposed job and time spent within the same industry or company in jobs that were not likely exposed. This allows for categorization of workers based upon the amount of time they were potentially exposed, usually quantified as either days or years exposed.

Person-Years Exposed (PYE) is the amount of years a worker spends in an occupation that is exposed to the exposure of concern. Table 6.3 gives an example of the type of *job exposure matrix* (JEM) that is needed in order to determine a PYE metric. The metric is time dependent with an assignment of exposure for each job and year combination in the study. As time progresses, a number of factors influence the intensity of an exposure, or even the presence of one in a workplace. The substitution of a chemical, installation of engineering controls, termination of a process or work area, and many other events can influence the exposure patterns across time.

The JEM is then linked to an individual worker's employment history in order to create the PYE for a worker. Table 6.4 gives an example of a hypothetical worker in a machine shop for potential exposure to solvents. For each year that the worker is employed in an occupation that has the potential for solvent exposure, they will receive one year of risk. If the worker is in different occupations throughout the time period of interest, then each job is evaluated and years at risk are totaled across occupations.

Table 6.4 — Person-Years Exposed for a Worker

Work History Year(s)	*Job Title*	*Potential Solvent Exposure (Years at Risk)*
1958–62	General Labor	No
1962	Machinist Helper	Yes (1)
1963–71	Machinist	Yes (8)
1972–1980	Machinist Leader	Yes (8)
1980–88	Machinist P&E	No
1989–90	Machine Shop Supervisor	No
Person-Years Exposed		17

Intensity or Average Exposure

The intensity or average exposure metric provides an overall average of the exposure of interest for a set amount of time (day, month, year, etc). This exposure metric is quite common in the daily routine of the industrial hygiene world as a time weighted average that is the primary compliance tool of measurement for many occupational exposure levels. It is a basic quantification of the amount of exposure a worker receives during a set amount of time.

In reconstructing occupational exposures, the overall average exposure is normally derived from these daily TWA measurements taken throughout the years. While industrial hygiene samples are not normally taken every day of a process, these TWA measurements can be summarized to produce an average exposure, (i.e. for a job title during a year). The average (either geometric or arithmetic) of these TWA measurements is then used as the overall average for that particular job title and may be used as an exposure surrogate for similar job titles that do not have exposure data available (discussed in greater detail in Chapter 7).

Lifetime Average Exposure (including unexposed jobs)

The lifetime average exposure metric is the overall average exposure that a worker receives in during their working lifetime including both exposed jobs and unexposed jobs. This metric is beneficial when examining the relationship between chronic disease and long-term exposures. Lifetime averages can include almost any exposure variable such as airborne concentrations (ppm or mg/m^3), radiation (REM), noise (dBA), etc.

This lifetime average, however, can be heavily influenced by background or non-exposed jobs. An example is given in Table 6.5 which calculates both the lifetime average exposure including and excluding jobs that were categorized as having no exposure to the solvent of interest. When including the non-exposed jobs, the lifetime average was 2.8 ppm but excluding them produced a lifetime average of 5.6 ppm. While this is just a hypothetical situation one can see how dramatic a difference can be made by either including or excluding jobs that are considered non-exposed.

Table 6.5 — Lifetime Average Exposure Calculation for Solvent Exposure

Work History Year(s)	*Job Title*	*Solvent Exposure (ppm)*
1961	General Labor	No
1962	Machinist Helper	Yes (6.5 ppm)
1963	Machinist	Yes (5.0 ppm)
1964	Machinist Leader	Yes (5.3 ppm)
1965	Machinist P&E	No
1966	Machine Shop Supervisor	No
Total Exposure		16.8 ppm
Total Years		6
Arithmetic Average Lifetime Exposure (excluding unexposed jobs)		5.6 ppm
Arithmetic Average Lifetime Exposure (including unexposed jobs)		2.8 ppm

A lifetime average exposure is a great metric for giving an overall view of exposure and can be found in the literature describing overall exposure patterns.[8] The inclusion and exclusion of non-exposed jobs is perfectly suited to a *sensitivity analysis* in the epidemiological analysis.

Lifetime Cumulative Exposure (Duration x Intensity)

The lifetime cumulative exposure metric is one of the most common exposure metrics used in reconstructing occupational exposures. It addresses two main concerns in exposure patterns: duration and intensity. For this metric the exposure intensity must be characterized by each time period (normally years). Each time period is then linked to the work history of a worker and the lifetime cumulative exposure is calculated for each individual worker in the cohort. Table 6.6 provides an example of the calculation of a lifetime cumulative exposure for TCE in a manufacturing facility. For each year of work history an exposure intensity variable is assigned and all years are summed to create the cumulative exposure in terms of parts per million-years (ppm-years).

Table 6.6 — Calculation of ppm-years for TCE exposure*

Work History Year(s)	*Job Title*	*TCE Exposure (ppm)*
1961	General Labor	No
1962	Rubber Worker	Yes (6.5 ppm)
1963	Rubber Worker	Yes (5.0 ppm)
1964	Rubber Worker	Yes (5.3 ppm)
1965	Manufacturing Assistant Manager	No
1966	Manufacturing Assistant Manager	No
Total Exposure		16.8 ppm–years

* Hypothetical data for this example. Not based on real monitoring data for TCE.

Rinsky et al. utilized ppm-years in a sentinel paper establishing the relationship between benzene and leukemia.[9] Another common variable is mg/m^3-year that was utilized by Checkoway in evaluating crystalline silica exposure.[10]

Duration of Exposure above a Specified Intensity

This metric might be useful to evaluate the difference in health outcomes for those ever exposed above "X" ppm versus those never exposed above "X" ppm. This may require dividing a person's work career into different jobs over time, with ratings for each job. Then, if different exposure intensities apply, this particular metric could be developed. This metric has some commonalities with the Peak Exposure metric discussed below.

Peak Exposure Levels

As discussed in the Ever/Never section of this chapter, the definition of "ever" is a very important factor in the exposure metric. So is the case with peak exposure. There are multiple ways to define peak exposures and a number are available in the literature as examples. The most important factor in determining the peak exposure metric variable is clearly stating early in the process what the definition of "peak" will be for the exposure assessment.

One definition of peak exposure is the highest average exposed job that a worker assigned. While the value is still an average exposure it is considered a peak value because it is the highest average exposure obtained by the worker. This peak metric was utilized by Sanderson et al.[11] when examining the relationship of beryllium and lung cancer and Meredith et al.[12] when examining the relationship between isocyanate exposure and occupational asthma.

Peak exposure can also be defined as the highest exposure ever received and can be determined a number of different ways. The average exposure is commonly used as an exposure metric, but if the multiple exposure data points (for example multiple time weighted average (TWA) values for a given job title) used to calculate the average are available then the highest data point can be assigned as the peak value. For example, if multiple TWA values are available for a given job title, then the highest TWA value could be assigned as the peak value with the average of the TWA values being assigned as the average exposure metric.

Task-based exposure data can also be used to determine peak exposure levels. Task-based industrial hygiene samples were more prevalent due to limitations of sampling equipment, so many long-term exposure assessments may have access to some type of task-based exposure data. With improvements to sampling equipment, longer sampling methods were developed and the use of TWA's became the normal practice. But with average 8-hour exposure, data plotting the peaks and valleys of exposures that occur during the daily work activities are lost and only reported as an overall average.

There are limitations with task-based exposure data, including the validity and use of these types of peak values. One school of thought is to simply use

the value "as is" with no modifications. Despite the short duration of the sample, ranging from a few minutes to a few hours, this thought process is that the sample accurately represents the peak exposure for that job tasks.

Other schools of thought attenuate these peak values, arguing that the absolute peak value only represents a very small portion of exposure. If the exposure pattern is viewed as a normal (or bell) curve, then this peak value would be on the extreme far right of the exposure curve. A percentage of the peak value, such as 90 or 95 percent of the peak, can be used to represent the peak exposure that would occur more often in a job task as opposed to strictly using the peak exposure point at face value. This represents another scenario where a sensitivity analysis in the epidemiological analysis could be explored if the exposure data permits.

Another variable of peak exposure is the frequency of peak exposure. Again, the definition of "peak" is of paramount importance. Once this is determined, the frequency of peak exposure can be characterized as the number of peak exposures per day, week, year, or any time period desired. Wong et al. used the number of peak exposures per day when examining the relationship between petroleum worker exposure to gasoline and multiple myeloma, kidney cancer, and leukemia.[13]

Determining Set Points for Exposure Metrics

Qualitative ranges and semi-quantitative ranges are perhaps easier to set if anchor points are considered. For example, even though data is too limited to firmly set the boundaries, "no exposure" might be thought of as population background. These are the workers that you would not expect to have any exposure, for example, a member of the administrative staff that never spends time in a production area. The background group can then be set at a nominal determinant, such as less than 1% of the occupational exposure limit (OEL). The next exposure group would then be characterized as the "Low" group with exposures between 1 to 10% of the OEL. Workers who have moderate exposures would be classified into the "Medium" category set at 10 to 100% of the OEL, and workers who have potential to be exposed at greater than the OEL would be receive a "High" exposure assessment assignment. Many studies have used categorical exposure ranges, for example Stewart et al.[14] and Schubauer-Berigan et al.[15]

Multiple Exposure Metrics

Multiple exposure metrics can be chosen when determining which metric is most appropriate for the exposure assessment being undertaken. However, it is not uncommon to design an exposure assessment strategy with multiple exposure metrics included for the same exposure of interest. For many health outcomes, the key exposure metric may not be known, so an evaluation of many different metrics may be needed to properly evaluate the relationship between exposure and disease. It is not a foregone conclusion that chronic diseases are always associated with long term exposures, nor acute diseases are always associated with short term exposures.[16] In epidemiological studies, the JEM is often composed of a number of these exposure metrics and the epidemiological analysis uses each metric differently.

In general, an average exposure is assigned for each combination of job title (or collapsed job title) and year in the study period. A peak value can also be assigned for each combination if the appropriate exposure data is available. Once an exposure assignment (average, peak, qualitative assignment, etc) has been made for each combination of job and year, then the JEM is complete and ready to be linked to each worker in the cohort.

An example of multiple exposure metrics is given in Table 6.7 that illustrates quantitative exposure assessments for three years. The example contains four exposure metrics. For each job and year combination, an average exposure is calculated from a number of TWA samples taken during the respective years. The arithmetic mean of the three years for each job title is calculated providing a lifetime average for each job. The peak is determined as the highest average TWA and is then determined for each job. And finally, a cumulative exposure is calculated by summing the average exposure for each job across the study period (only three years in this hypothetical example) and providing the final exposure metric of ppm-years or a lifetime cumulative exposure.

By providing multiple exposure metrics in the JEM, the epidemiologic analysis can evaluate each variable and its relationship or non-relationship with the health outcome. Multiple independent exposure metric variables could be used in the epidemiological analysis to gain insight into relationships between variables, which exposure variable is a better predictor of health outcomes, or if no variable was predictive. However, the JEM should only contain exposure metrics that can be appropriately supported by the exposure data available.

Table 6.7 — Quantitative Job Exposure Matrix (JEM) with Multiple Exposure Metrics

Job Title	1968	1969	1970	Arithmetic Mean (PPM)	Peak (PPM)	Cumulative (PPM)
Job A	7.9	9.9	4.6	7.5	9.9	22.4
Job B	6.3	6.2	5.5	6.0	6.3	18.0
Job C	3.4	2.7	2.2	2.8	3.4	8.3

Confounders and Effect Modifiers

Almost all epidemiological studies will have to address the concern of potential confounders and effect modifiers. All of the exposure metrics discussed in this chapter are applicable to confounders, effect modifiers, or any other exposure of interest. They are not reserved only for the primary exposure. However, often times it is the case that the primary exposure will have the best exposure data available, but it is not always the case. Many exposure assessments contain a number of different exposure metrics, including both quantitative and qualitative assessments.

For example, when Yiin et al.[17] evaluated the relationship between ionizing radiation and cancer outcomes, the exposure records for ionizing radiation were far more complete than any records for potential confounders such as benzene or smoking. Since ionizing radiation was a major health concern from the beginning of the use of nuclear reactors on submarines, the radiation badge records were well-maintained and archived. Conversely the industrial hygiene records for the use of benzene at the facility were very limited and almost no monitoring data was available. Even though a very thorough exposure assessment could be completed for the ionizing radiation, only a quite elementary exposure assessment could be completed for the confounding exposures. Despite the differences in the amount of exposure information available for each exposure, both metrics could be used in the epidemiological analysis to evaluate the relationship between ionizing radiation and cancer outcomes.

The use of quantitative, semi-quantitative, and qualitative exposure metrics in the same study is perfectly acceptable. Table 6.8 illustrates the use of both quantitative and qualitative exposure metrics in the same JEM. The primary exposure of interest (e.g., TCE) had enough exposure data available to create a quantitative estimate of exposure, while the confounding exposures only had a limited amount of exposure data available and were only able to provide an ever/never exposure estimate.

Exposure Patterns

For exposure reconstructions for litigation, workers compensation, etc., exposures associated with upset conditions and other significant excursions can be important to understand. The biological basis for concern (that is, level of acute exposure relevant to the end effect of concern), relevant metrics, relative magnitude and frequency should be established as part of the study design.

The industrial hygienist may be asked to estimate exposures other than long-term averages (LTA) for other than litigation. For some hazards and epidemiology studies, information on the pattern of exposure might be important in establishing the health risks. For acute toxins, such as hydrogen cyanide, the short term peaks may be much more relevant than an LTA such as an annual average. On the other hand, for chronic toxins, like lead, the typical short-term "peaks" within a day may be largely irrelevant, and the LTA may be the most important metric. The relevant exposure patterns to investigate should be established in the study protocol. It is the biologically relevant pattern that needs to be considered. This may be different from the OEL definition of peak or regulatory "peak" exposures. Episodically elevated exposures may be a concern, too, such as exposures that occur during unusual or infrequent events. If the routine monitoring data is sufficiently large in number and covers the breadth of the operation's variability, then the statistics of the data distribution can be used to understand the expected frequency of exposures above a specified value.

Some operations, such as refinery maintenance, have typical routine repair activities and thus routine exposures. However, production equipment is shut down for major maintenance, called turnarounds, possibly once every several years. During these times, the exposures are of a different nature, and

Table 6.8 — Quantitative Job Exposure Matrix (JEM) with Confounding Exposures

Job Title	1968	1969	1970	TCE Arithmetic Mean (PPM)	TCE Cumulative (PPM)	Benzene (Confounding)	Carbon Tetrachloride (Confounding)
Job A	7.9	9.9	4.6	7.5	22.4	YES	YES
Job B	6.3	6.2	5.5	6.0	18.0	NO	NO
Job C	3.4	2.7	2.2	2.8	8.3	YES	NO

may be of different magnitude than during the routine operating maintenance. Some operations will have historic measurements for these turnarounds.

In some instances, the goal is to estimate exposure during spills of materials, cleanup of these, or during other non-routine situations. Then, mathematical modeling[18] may be an important tool. Sometimes the IH may be able to estimate practical upper limits based on IDLH or substance warning properties, but these approaches have limited use and significant uncertainty.

Exposure Concentration versus Exposure Dose

Depending on the rigor of the quantitative risk assessment goals, the IH may need to consider possible dose and factors affecting it, rather than just estimating the air concentration. Some of the aspects include, integrating all relevant routes of exposure, addressing differences in hours worked over time, or even level-of-exertion during exposed jobs. For some exposure situations, physiologically based toxicokinetic models (also referred to as physiologically based pharmaco-kinetic models) may be useful in understanding the delivered and retained doses.

Biological Markers of Exposure, Biological Exposure Indices®

The utility of biological exposure markers depend to a large degree on the validity and quantitative basis of the marker. The ACGIH® BEIs® are well evaluated and their associated documentation will guide the IH on their application and interpretation. There are also markers of exposure that have not been validated, or that may not relate well quantitatively to exposure. Markers of effect may or may not relate to exposure, since some may be caused by exposure other that to the study hazard.

Exposure Assessment Uncertainty Evaluation and Confidence Ratings

Although not specifically an exposure metric, an indicator of the certainty of (or confidence in) an exposure assessment can be a useful adjunct to the exposure metrics. Perhaps some of the TCE exposed jobs had extensive and reliable data of high quality. Other jobs, although likely exposed to similar intensity, may have had much less reliable data. One may chose to give them the same rating for intensity. Providing a rating on the IHs "certainty" will provide useful information for a sensitivity analysis. That is, the epidemiologist may do an analysis including all of the subjects with their assessed exposures. Then, a subsequent analysis may drop out those subjects with the lowest EA confidence ratings. This is to check if the study results remain the same, increase, or attenuate with the less certain exposure assessment data. More discussion on confidence ratings follow in Chapter 8.

Chapter 7: Develop Exposure Estimates

As discussed in prior chapters, the exposure assessment details must align with the design of the overall study and the epidemiology analytic plans. The final exposure assessment details must align with the available information, such as work histories, manufacturing/worksite factors, and whatever quantitative or qualitative exposure data are available. When performing reconstructions for epidemiology studies, the exposure results need to cover the study population with as minimal exclusion of subjects as possible. In this section, aspects of completing the exposure assessment process, and several exposure reconstruction approaches will be discussed. These include:

1. Job-Time-Exposure or Task-Time-Exposure Matrices
2. Ever/never exposed
3. Qualitative, ordinal ranges when data are insufficient for more quantitative ranges
4. Quantitative exposure estimates based on exposure measurements
5. Expert panel assignment
6. Self-reported exposures
7. Considering all routes of exposure, air, dermal, other.
8. Contending with gaps in available data
   a. Estimations based on modeling
   b. Physical recreation of work environment, materials and then measurement
9. Handling the exposure assessment data
10. Documenting the exposure assessment process and its strengths and limitations

Which exposure assessment approach is used depends on the study goals, deadlines, staffing and on the availability, quantity and quality of the data. The various approaches described in this chapter may share certain key data, but the level of detail, and breadth of the information needed varies. The list above can also lead to combination designs, such as a study using self-reported (by study subjects) exposures as "ever exposed, never exposed" with subsequent refinement by the industrial hygienist to qualitative (no, low, medium, or high) categories. The IH may be asked to review the self-reports and assign a "confidence" in them based on their knowledge about the work history and industries. The confidence scores can subsequently be used in sensitivity analyses of the data. Chapter 8 further discusses confidence scores and sensitivity analyses.

These various exposure assessment options can be applied to individuals or to groups, either directly or via job or task-exposure-time matrices. From these assessments and information on how long study participants held particular jobs, one can derive the main metrics agreed to for the study design. (See Chapter 6 for further discussion of exposure metrics).

The references cited in this chapter are examples, and do not represent comprehensive coverage of the aspect. See Attachment A for relevant general references not specifically cited within this chapter.

Job-Time-Exposure Matrices and Task-Time-Exposure Matrices

Besides exposure reconstructions for only one or a few individuals, most often an industrial hygienist will need to assess the exposures for many individuals holding a range of jobs in one or more industries or facilities over a multiple decade time period. In such cases, job or tasks-based exposure matrices are a commonly used tool. There is a wealth of literature on constructing Job Exposure Matrices, which may more broadly be called job/task, time period, exposure matrices. Job-exposure matrices (JEM) as originally developed and used[19] depend on standard job definitions, an assessment of exposure for each, and then linking the study subjects work histories to the JEM. Task Exposure Matrices (TEM, see further discussion below) may also be used. The JEM (or TEM) may be very general with respect to the number of jobs and their descriptions, or it may be much more detailed. The exposures assigned to the job cells in the matrix can be broad such as "ever exposed, never exposed", or with a qualitative scale (not exposed, low, medium, high exposure), or with quantitative estimates of exposure. Compilation of job and exposure information, such as from the NIOSH National Occupational Exposure Survey[20] national "exposure" databases[21,22] or general texts (see Chapter 8 and Attachment A) may be useful for the general qualitative characterizations of exposure, and perhaps for rudimentary quantitative assessments. More specific quantitative exposure infor-

mation is likely necessary for quantitative JEM construction. For some materials, for example hydrocarbon solvents, general reviews and compilations may exist to help guide the JEM formation. Thus, you might find a wealth of useful information from a thorough literature search for what others published for the industry, jobs, or exposures of interest.

Obviously, not all people assigned to a JEM cell had the same actual exposure, which is a well-recognized issue with traditional JEMs where there is no differentiation of those assigned to the same job cell. For example, in the beryllium-using bicycle factory, some work groups have no direct exposure. However, with a factory-level JEM design, it may be that all people who worked in any job in a factory known to use beryllium would be assigned to the "exposed" cell. A possible enhancement on this might simply be sorting out "likely unexposed" jobs with clerical or managerial titles. Assignment of individuals with infrequent exposure in a job or specific task to the same exposure category as those frequently exposed can result in misclassification of exposure, and may compromise the studies' findings. In the beryllium example, assigning the supervisor who spent roughly 10% of his time at fill-in production work to the same level as those exposed full-time could be problematic. Quantitative and semi-quantitative JEMs should also consider different cells for a given job to reflect the likelihood of long-term changes in exposure.

Task-based exposure matrices (TEM) may better define exposures for individual subjects, if information on the frequency and duration of the tasks for the jobs to be assessed is available. A task-based exposure matrix may also employ standard task definitions, with the number of tasks and their specificity depending on the study design and supporting information. Alternatively, a JEM may be modified to better fit job differences based on questionnaires or other sources of information about exposure modifiers for individuals.

When information is available to support the details, time periods for the exposure estimates should be driven from known changes in processes, exposure controls, and other factors that modified exposures. Arbitrary divisions, such as 5-year periods, or decades, if associated with differences in exposure, nevertheless may be better than keeping estimates flat over decades where changes were likely.

Ever Exposed, Never Exposed

By this, it usually means that people had opportunity for occupational exposure, or did not have jobs that could have led to exposure to the hazards of concern. Note that for very low exposures, criteria must be defined for exposed versus non-exposed (see Chapter 6). This (ever exposed, never exposed) type of exposure reconstruction is most often used to establish whether a relationship exists between a hazard and a health outcome. Ever/never exposed designs do not give data for quantitative risk assessment, and do not help define a dose-response relationship, which limits the utility for setting quantitative risk-based limits. A simple combination with the years in the possibly exposed jobs gives the metric duration exposed.

Some studies had added a "probability" of exposure with the ever exposed, never exposed design. In some of the studies, the probability was based on an assessment of the prevalence of exposure of personnel in an industry. The NIOSH NOES[7] has been used to set the exposure prevalence. Probability for a group can give substantial exposure misclassification, because the prevalence for a group may not represent an individual accurately. Subjective probability scores assigned by expert opinion might also be used with an ever/never exposed design. The probability rating scale should be defined in advance with the investigative lead team. Criteria should be clear to help guide consistent application. Such probability ratings can be used in sensitivity analyses where the outcome associations are checked by first including all subjects, then selectively dropping out those with lower probability scores, to see if the results remain or attenuate.

Semi-Quantitative and Ordinal Scales

Qualitative ranges (e.g., no, low, medium or high exposure) and semi-quantitative ranges are perhaps easier to set if anchor points are considered, as suggested by Stewart.[23] These "anchor points" of relatively robustly assessed jobs and exposure levels can strengthen the relative ranking of other jobs in an industry or job category in a qualitative or semi-quantitative scale JEM or TEM. A main goal of this ordinal scale or semi-quantitative approach is rating the jobs correct relative to the other jobs in the study. That is, can the IH be sure that the high jobs are the most exposed, with medium exposed lower, but above the low exposure jobs? If data is too limited to firmly set the boundaries on the categories, one might think of "no exposure" as population background (<1% of the OEL), low as 1 to 10% of the OEL, medium as 10 to 100% of the OEL, and high as > 100% of the OEL. Many studies have used categorical exposure ranges.

Exposure Reconstructions with Quantitative Exposure Measurements

Exposure reconstructions based on exposure measurements need to consider how well the measurements cover the relevant jobs, tasks, and relevant years for the study population. There are many other considerations in the use of measured data as well. The following applies to air concentration measurements primarily, but may also apply to valid biological exposure indicators, such as ACGIH® BEIs®. Note that not all biomarkers of exposure relate well quantitatively to past exposures, but may indicate rather that an exposure to an indeterminate quantity had occurred.

The extent of the available data and the extent of documentation for the data are fundamental aspects in exposure reconstruction, and determine the possible apportioning of the total data into subsets by time, or job/task. The data quality depends on the original survey strategy, its documentation, and on the validity of the sampling and analytical methods, and for laboratory analyses, on the laboratory's proficiency. For data sets extending over considerable years, the data quality and other details may have changed. If so, and if possible, a translation/correction table may help improve the use of the "lesser quality" data. Statistical comparisons of the different segments may also have a role in determining if changes over time are significant. A detailed discussion of the statistical analysis is beyond the scope of this chapter. As a starting point, it is suggested that the reader consult the statistical discussions of the AIHA books in Attachment A. For extensive, high-quality data sets, it may be possible to define intra- and inter-individual variability. For any project considering new surveys, these intra- and inter-individual difference may also be important investigational considerations. For additional information on the intra- and inter-individual investigation design considerations, see *Attachment A References*, Rappaport et al. 1995 and Kromhout et al. 1993. The discussions on data analyses within those publications cover many of the aspects mentioned briefly here.

Data Quality, Types, Summaries

Earlier in the project, the IH established what data is available. Now, when faced with using the quantitative exposure measurement data, some additional questions and review may be in order. Did methods change over time? Do differences in the results need to be considered? Do all the methods directly measure the hazard of concern, or do some of them represent a surrogate measure, such as total chromium when the hazard to investigate is hexavalent chromium? Were different sampling periods used, such as one-minute grab samples, task-length TWAs or full-shift TWAs? What survey strategies were applied — random, targeted, convenience? Were any of the data already stratified by *Similar Exposure Groups* (SEGs)? If the data were transferred from original records, such as into a computerized database, what processes were used to assure accurate transfer of the results? An EPA document[24] provides a good, general discussion on classifying occupational exposure data into different classes so that reliable data are identified and used as the primary quantitative basis.

An experienced industrial hygienist would probably understand how variable occupational exposures can be. That variability can arise from both within-worker and between-worker differences. Both can be important in quantitative exposure reconstructions, and may be considered if the data set provides enough well-described samples. Often, though, the IH will face trade-offs between specificity of the measured data to the worker and the job versus statistically robust numbers of samples.

Summary statistics for the data should include as much as possible, including AM, GM, GSD, n, confidence intervals (particularly for the AM) and duration of the samples (such as short term versus full shift). Other summary statistics may include interquartile ranges, upper and lower 95th (or 90th, 99th) percentiles of the data distribution, and confidence intervals on these parameters. The variability of the data can be used to estimate the frequency of exposures above the average, or above a selected upper limit, such as the OEL. However, for such inferential statistics, the nature of the data's statistical distribution should be verified, such as normal, log-normal, or neither. If neither, it may represent mixed distributions, or yet another type of data distribution. Non-parametric methods may also have a role in such situations. If the statistical complexities get to the point of contending with mixed distributions, or truncated distributions such as with prevalent limit of detection entries, the advice of a statistician with experience in these topics may be needed.

Summarizing the available data can help with the data's use and also helps document the information. A table (see example on the next page) can help organize the data.

If much data is obtained over time, graphing the data sorted by time may give insights on trends to evaluate further.

Data available for operations of interest may include short-term grab samples, 15-minute samples to evaluate STEL compliance, fractional shift or

Type	Number	AM	GM	GSD	Dates of Measurements	Comments (strategy, validity, other)
For Job _____(Describe)						
Area	____	___	___	___	From ____ To ____	_____
Personal TWA	____	___	___	___	From ____ To ____	_____
Personal Task 1	____	___	___	___	From ____ To ____	_____
for Task (describe) _____ frequency _____ (per day, week, year) Duration _____ (minutes per event)						
Personal Task 2	____	___	___	___	From ____ To ____	_____
for Task (describe) _____ frequency _____ (per day, week, year) Duration _____ (minutes per event)						
Personal Task 3	____	___	___	___	From ____ To ____	_____
for Task (describe) _____ frequency _____ (per day, week, year) Duration _____ (minutes per event)						
Sources of data summarized _____(list)						

task-specific time-weighted average samples, and full-shift time weighted average samples. There may also be several sampling and analytical methods used, especially for data that spans multiple decades. The short-term and time-weighted average data need to be segregated since they should not simply be averaged. Estimates of long-term average exposure are best if based on random samples from the study population, or from strata within the total population. However, IHs often select workers and situations to monitor, looking for higher-end exposures as an efficient strategy for evaluating OEL compliance. How these differ from truly random samples may be difficult to determine, but this will need to be considered this in the use of these data for exposure reconstructions. The IH "convenience" sampling strategy may often give an approximation to random samples since assessors often fail to catch the worst situations when sampling exposures, even when trying to do so. Most IHs have heard workers say more often than not "You should have been here yesterday!" Regulatory compliance databases can give insight into the magnitude of exposures to regulated substances in regulated and inspected industries. However, biases in how factories and workers were selected and how the regulatory presence may have perturbed routine practices are hard to discern and inarguably account for in use of the regulatory inspection data.

For operations where protective equipment was used to protect workers, you will need to resolve several issues. Most often, exposure measurements evaluate the air concentration, which with effective respiratory protective equipment (RPE) use can be quite different from the inhaled air concentration. Back through time, before the implementation and enforcement of regulations on respiratory protection, the RPE use, quality and effectiveness may have varied considerably from worker to worker, job to job, and industry sector to industry sector. Several reports give different approaches to adjusting for the use of RPE[25,26], but this may take considerably more investigation before an approach is decided upon. Biological monitoring results, if available, can be used to assess the success of RPE and other PPE use. Otherwise, the IH may sort through the magnitude of the issue by reviewing the strengths and weaknesses of the RPE use. When did the respirator program start? Was RPE use required or recommended? Can the % use (near 0%, near 100%, in between?) be estimated? Are biological monitoring data available for periods when respiratory protections were not used and when they were used? Is it possible to collect "in facepiece" air samples to compare to the air concentration data? Were different types of RPE used over time, such as ¼ face, half-face, or full-facepiece designs? For air purifying respirators, was there an adequate approach to cartridge selection and change-out intervals? Did the odor, irritation or other aspect of the air contamination help reinforce RPE use? Was there a routine inspection and maintenance schedule for respirators? Note that any of this information, if reliable, could be used to assign different "protection factors" over time to account for changes in the effectiveness of the RPE/PPE program. This list of questions is to help the IH get started in evaluating the RPE. The requirements for a good RPE program may be used as a guide to analyze how the program of interest performed.

Expert Panel Assessment

Expert judgment has been used in many retrospective exposure assessments. Broader discussions of expert assessments are available.[27–29] Key aspects of this method that will need to be resolved for this method include:

- Selection of experts, and assuring or building their expertise
- Calibration of the experts with any available information on exposures and changes over time
- Evaluating and resolving differences by different experts. Kappa and weighted kappa statistics[30] can help evaluate the differences between scores given by different experts.
- Validation of the results

The expert panel may assess the exposures for the various designs (ever/never, ordinal scale, quantitative, etc.) given sufficient information and time. Validation of an expert panel's assignments can be made by comparing the assignments to available data. For more detail on validation, see Chapter 8.

Self-Reported Exposures

An industrial hygienist has special training and experience in recognizing, evaluating (and controlling) exposures. If someone was conducting a study on industrial hygienist's exposures, their self-reported exposure assessments may (or may not) be more valid than the many exposure assessments studies conducted that rely on self-reported exposures of workers or members of the general public. The literature on self-reported exposures is somewhat diffuse and does not give a clear and universally applicable direction to maximize validity. Some studies suggest that industrial hygienist's assessments are not better than and sometimes not as good as self-reported exposures. Other reports suggest industrial hygienists, when assessing operations in their area of experience may perform adequately. With respect to self-reported exposures, generally, study subjects may reliably recall when they worked, where they worked, and might describe the industry. Some workers might know the common names of substances with which they have worked but may not know the chemical names of substances. Hazard communication and Right to Know regulations do not guarantee the workers know exactly what they worked with, or what their exposure levels were. Even so, recalling such information accurately from years ago can be difficult.

McGuire[31] suggests spending more interview efforts on understanding the jobs and tasks, and less on the specific exposures since the latter is often less than well known by the subjects. There have been concerns raised that workers who suffer the potential consequences of the exposure might be more likely to recall exposures in greater detail than those who don't (i.e. recall bias). On the other hand, workers who do not suffer those potential consequences might underreport exposures. These two issues would result in exaggerated risk estimates. However, Teschke[29] cites three investigations that suggested that differential recall by cases compared to controls has not been an issue.

Contending With Gaps in the Data — Surrogates

In exposure reconstruction, assessors almost always lack the ideal data. Given that, the IH needs to do what he or she can with the information available, and at times find creative solutions to bridge gaps in data. Surrogate measures may help fill data gaps if direct measures of the exposure concern are missing. Other exposures which likely co-varied with the exposure of concern, and for which data is available are considered surrogates. For example, if the early data on beryllium operations has some total dust measurements, it might be useful if the ratio of beryllium to total dust in the operations is established. The IH must be careful to check and comment on the relationship as valid and stable (or not) for the relevant periods.

Surrogate operations may also be informative. That is, an older facility which is still operating may give insights into the types and magnitudes of exposures in a study facility that has closed or undergone major changes. This does depend on the relative equivalency of the operations, because if the one is not an adequately accurate good surrogate, the findings may be misleading. Even the equivalency of feedstocks and additives in the process might need to be evaluated, since modern materials may change the nature of exposures, even if the operating equipment is similar to that used in the more historic operations you are attempting to understand.

Contending with Gaps in the Data — Simulations of Past Jobs, Tasks

The IH may encounter situations where there is no available relevant exposure data, for the exposure of concern or for suitable surrogates. An option, but not one to undertake lightly, is recreating (simulating) past situations and measuring the resulting exposure potential. A number of issues need to be addressed including:

- The ability to accurately establish the workplace conditions (size, ventilation, process technology, other materials)

- The availability of the exposure agent in relevant to the period formulation, or feasibility of using a surrogate material
- Protecting personnel engaged in the simulation
- Determining the extent of monitoring needed to reflect the exposure variability, including seasonal issues
- Establishing task performance and how to assure the work is done as it had been.

Often, the IH will need considerable resources and budget for successfully completing such historic simulations. Capturing the exposure determinants (contaminant generation rate, ventilation, temperature, task duration, etc.) is important since this can be useful with appropriate mathematical models to extrapolate the simulation findings to different conditions.

On occasion, industrial technology museums and older technology journals may provide information on the processes and conditions to simulate. If done on a reduced scale, the validity of extrapolation to full scale conditions may be difficult to verify.

Contending with Gaps in the Data — Modeling

There are many categories of models that can be useful in retrospective exposure assessments. Deterministic physical/chemical mathematical modeling, regression models based on available data, comparative models based on determinants of exposure, and expert system designs are some of the possibilities. Full discussion of them is beyond the scope of this guideline. For more information, see Attachment A Essential References (Keil 2000, Ignacio and Bullock 2006).

Predictive modeling based on physical and chemical properties, contaminant generation rate, methods of use and controls in effect.

Here, the simpler models and simplifying assumptions may be applied first.[18] The available details on the operation (room size, ventilation, material composition) may dictate the extent of modeling possible. There are courses on predictive modeling available, and various modeling tools, ranging from spreadsheets to commercial software. A few of the simple models used by industrial hygienists include:

- Saturated vapor concentration
- Simple box model
- Gaussian plume dispersion
- Eddy diffusion model
- Near field/far filed (two zone) model

Stochastic methods can use probability distributions of the factors in exposure assessment models. This approach has not yet been widely used in retrospective exposure assessment, but has been demonstrated[32,33] and provides some advantages including the uncertainty analyses most Monte Carlo simulation software packages include. It is also useful at times when exact values for input parameters are difficult to determine, but where credible ranges can be estimated. At a higher level in modeling, computational fluid dynamic (CFD) simulations can help estimate exposures but CFD requires a great deal of data about the physical layout and ventilation of a specific worksite.

Predictive and/or comparative modeling based on operating system description and method of use, with limited (semi-quantitative) consideration of the physical/chemical properties

This approach relies on a comparative process and considers, qualitatively, the volume of material, proximity to people, degree of containment, system temperature and pressure, and other factors to subjectively rank the potential for exposure. If containment is complete and exposure opportunity during sampling and other open systems operation is nil, then the overall exposure is nil. If the systems are open, use relatively high vapor pressure materials, and controls are absent, the exposure may be rated "> OEL." This may be an adequate approach for the first assessment, but may require later refinement via more detailed modeling.

All Routes of Exposure — Dermal Exposures

Dermal exposures can be particularly important for non-volatile and low-volatility chemicals. Generally, unless good RPE was used in high-exposure air concentration, vapor-phase dermal exposure is not a major contributor, except for a few particular substances. Otherwise, the extent, frequency, and duration of skin contact should be investigated. Transdermal penetration of very fine particulate could be a hazard in some operations, including with nanomaterials. It may have been a factor with beryllium. Several screening models can help the IH understand the role of dermal contact ion the total exposure. The UK HSE-developed model EASE[34] can help find the range of dermal loading in mg/cm^2 per day or per event. This can then be used with a conservative default "all absorbed" assumption to decide on how relevant the dermal route could be. If relevant, additional effort can be spent to better estimate the dermally absorbed dose.

The model SkinPerm[35] may help estimate the absorbed dose for organic compounds. Note that there are additional dermal absorption models available and SkinPerm may or may not fit your project needs. Semi-quantitative estimation may be considered, with one approach described by de Joode.[36]

Determinants of Exposure and Modeling

Determinants of exposure are those aspects that allow for contaminant release, transport, and "uptake" by the workforce. That is, how is the contaminant released to air, and in what quantity? Then, how does the workplace environment enhance or mitigate the dispersal of the contaminant? Lastly, how do the job's tasks (frequency, duration) lead to the presence of workers in the contaminated zone? An understanding of these gives insights into the causes of and ways of controlling current exposures. Information on how the determinants changed back through time can be used in modeling past exposure from current data. To do this, you must establish what the key determinants are, and how to use them in modeling. Although broad categories of determinants might be defined, the key ones for a particular operation can be somewhat specific to the situation. Generally, the quantity and composition of the contaminant source material is important, as is how and in what quantity it is released to the work environment. Then, the quantity and quality of ventilation is key, as is the presence of other contaminant sources in the workplace environment. Further, how does the workforce interact with the contaminant source, such as the distance from and time spent in the zone (that is task duration, frequency, and distance from the source). Use of personal protective measures and work practices may also be in the list of key determinants. For further information on approaches to studying the determinants, and listing of studies using the approaches, see Attachment A: Essential References (Burstyn and Teschke 1999 and Teschke et al 2002).

All Routes of Exposure — Other (Ingestion, Injection)

Total Human Exposure assessments that consider and integrate all routes of exposure are more often sought in general population studies, and less seldom in occupational studies. Nevertheless, there are situations where these routes need to be considered. Generally, it will be for semi-volatile or non-volatile substances. For example, if the IH has the task of assessing the lead exposure potential for utility workers (electrical, telephone, etc.), they should evaluate hand hygiene before smoking or lunch/snack breaks. In such situations, biological samples, if available, are invaluable.

Exposure Patterns, Exposure Concentration versus Exposure Dose

Chapter 6, which deals with exposure metrics, discusses exposure patterns and how they may be important in some studies. It also provides some discussion about exposure dose estimates versus external exposure concentration estimates.

Handling the Data

For individual assessments of one or a few individuals, the recordkeeping and calculation issues should be tractable in any manner. For larger studies, that often cover hundreds or thousands of workers, jobs history segments, or tasks, the recordkeeping and calculations will take considerably more planning and resources. Many epidemiology studies have personnel dedicated to the data management aspects. As the industrial hygiene member of the team, one should engage early in the project development with such other team members to plan and coordinate the IH and exposure information handling.

Documenting the Exposure Reconstruction Process Applied

While completing the estimation process, the IH should be familiar with the validation process and QA/QC methods in order to organize and appropriately document the assessment to support these important study aspects. Some of the points to look at include internal consistency of jobs and time periods for the study population, sensitivity analyses, confidence ratings (and rationale for the confidence) on the estimates, and comparisons to any prior similar studies. Writing down a frank listing of the strengths and limitations can be beneficial to others' understanding of the generated data. See Chapter 9 for further discussion on documentation and record keeping.

Examples from Scenario 1 — Beryllium

The beryllium scenario lists key tasks associated with exposure. When starting the investigation, all that is available is a summary report prepared for the

company management that provides the average data for the period 1982 to 2007. The report states "For the 111 beryllium in air samples, the average is 0.9, the median 0.12, the minimum 0.002 and the maximum 50 mg/m^3." What can be done with this less than ideally informative summary? This does not discuss the survey strategy (e.g., typical conditions or worst case), whether they were personal samples, area samples, a mix of the two, short term or full shift samples. The IH can say there was beryllium exposure, and some in excess of current standards. If a summary statistic must be chosen, is the average or the median used? The average may be greatly influenced by unusually high non-typical samples. The median means half the samples were above this value and half were below it. Is this the better choice? Arguably, yes, since the data set is rather heterogeneous, covering many jobs, tasks, and time periods. If the data were from a similar exposure group in one stable exposure period of time, the answer could be different. The mechanisms of toxic response may also be a consideration, in that if high occasional exposures matter, then the median may not be the best metric. We know, however, that these example data are of rather uncertain quality and applicability. Fortunately, the investigation continues.

After a few days searching in files, you find the original survey reports are found and a more satisfactory summary of past exposure monitoring can be developed. There is data available on exposure to beryllium or a surrogate for each of the major tasks, in typical operating conditions, so a task-job-exposure matrix makes sense. Let's presume one decides to start with arbitrary (for now) 5 year periods. The IH realizes these periods can be adjusted later on to better fit any actual changes in specific periods that a more detailed investigation suggests.

Job History Information Examples

1. Joe worked from 1975 to 1995. He started and finished as a machinist doing threading work. At first, all the work was with steel. He remembers the introduction of beryllium in 1982. For the first 5 years, it was only about 25% of the work. Later, he worked only with the beryllium alloys. Setup took about 30 minutes at the beginning of the shift. Cleanup at the end was another 30 minutes.
2. Sam worked as a welder from 1966 to 1996. Before 1982, he welded just steel. In 1982, he specialized in welding the beryllium materials. He said several others specialized too, and others worked mainly with steel, but sometimes beryllium depending on orders. They switched to a new welding process in 1990 that reduced fume exposure and increased production. Sam retired in 1996.
3. Phil's last 15 years was as a supervisor who did about 70% administrative work and otherwise did fill-in work for whatever needs to be done, but that seldom involved threading or welding. Mostly the fill-in he did was shaping, grinding or polishing, and he guesses each was about 10% of his time. Phil retired in 1997.

Note: Hypothetical Data for this Example (not from any real beryllium samples)

Task	*2002–2007*	*1997–2002*	*1992–1997*	*1987–1992*	*1982–1987*
Shaping	N=10 AM= 0.02	N=10 AM= 0.03	N=6 AM= 0.04	N=4 AM= 0.06	N=3 AM= 0.09
Grinding	N=12 AM=0.15	N=4 AM=0.6	N=7 AM=0.12	N=0	N=2 AM = 2
Threading	N=3 AM= < 0.002	N=0	N=0	N=0	N=3 AM= 0.005
Welding	N=5 AM=0.02	N=5 AM=0.05	N=5 AM=0.1	N=5 AM=0.2	N=5 AM=0.2
Polishing	N=6 AM=0.4	N=6 AM=0.4	N=6 AM=0.4	N=6 AM=0.4	N=3 AM=1.5 Total dust)

N = number of samples
AM = arithmetic mean, ug/m^3
All as STEL, 15 minute monitoring results

Exposure Assessment Examples

1. Ever exposed/never exposed. Using this method, Joe, Sam and Phil are all assessed as "exposed." The assessor may break the work histories into "unexposed" prior to 1982 as a simple refinement.
2. Qualitative Scale. For the first part of this example, let us assume we do not have the quantitative data from the table above. All we know is from the work histories, and a general knowledge on the history of beryllium at the factory. You also know from general reading that grinding, polishing, and welding caused higher exposures than threading.

   Prior to 1982 all "no exposure"

   Joe. Between 1982 and 1987, his exposure was lower than post-1987, due to the lower volume of work with beryllium. Without measurement data, this is difficult to assign with certainty, but it is a lower exposure than for Sam.

   Sam. Between 1982 and 1990, Sam had significant exposure as a welder. Post 1990, his exposure was lower than previously. Uncontrolled welding resulted in excessive exposure, above the OELs of the period. So, the period from 1982 to 1990 can be rated as "high" and post-1990 as "moderate".

   Phil. Since Phil worked as a supervisor, the first thought might be to rate Phil as "no exposure." However, the notes that say he did production work at some significantly exposed tasks about 10% of his time. The decision is to rate his exposure as "moderate" since it is about 10% of that of the full-time workers in the jobs Phil did part-time.

3. Quantitative Scale. For this part, one has access to all of the data shown in the table. Obviously, there are some significant gaps, but this is what exists. All in all, most industrial hygienists who have done exposure reconstruction might call this a remarkably complete record.

   Joe. Although there are only 3 measurements in 1982 to 1987, they confirm the reading of the literature from other investigations of beryllium machining that threading was a low exposure job. Further, the survey reports say the samples were all from normal operating periods, when working with beryllium. This job was steady during the day, between setup and cleanup. There is no reason to think the operations were different between 1987 and 1995, when Joe retired. The samples are short term exposure limits (STEL) (15 minute samples), and should be the same. However, Joe's TWA went up with the change to full-time work with beryllium in 1987.

   1982 to 1987, STEL 0.005 ug/m^3, TWA 7/8 x 1/4 x 0.005 = 0.001 ug/m^3

   1987 to 1995, STEL 0.005 ug/m^3, TWA 7/8 x 0.005 = 0.0044 ug/m^3

   The three samples do not give a good measure of the GSD, so directly calculating the confidence intervals is problematic. One might consider pooling the GSD estimates from other samples in other operations for use in estimating the confidence interval for threading.

   Sam. Sam's exposure would appear steady from 1982 to 1990. There is information that says the controls improved in 1990 and reduced welding exposures from then on. The data for 1990 to 1992 is mixed in with some prior years' data, and the raw data are not available. In this instance, you note the 1992 to 1997 data are lower, and decide to use them back to 1990. Although not included in the IH survey reports, you have other information that suggests the actual welding time was limited to about 5 hours a day.

   1982 to 1990. STEL 0.2 ug/m^3, TWA 5/8 x 0.2 = 0.13 ug/m^3

   1990 to 1996. STEL 0.1 ug/m^3, TWA 5/8 x 0.1 = 0.06 ug/m^3

   Phil. He became a supervisor in 1982, and held that job until retirement in 1997. His work was 10% grinding, shaping and polishing for those 15 years between 1982 and 1997. For grinding, the gap in the data for 1987 to 1992 might be better handled by a simple average of the date before and after, or 1.1 ug/m^3. Without further information on what changed and when it changed, this "average the before and after" levels may be all that one can reasonably do. The STEL assessment, if needed, becomes more complicated, since Phil had STEL exposures and all of these jobs. The assessor may choose to report the average, with the lower and higher jobs as ranges on the job. Phil's long term TWA exposure may be divided into the three time periods. By time period:

   1982–1987, [(0.09 +2 +0.4)/3] x 1/10 = 0.083 ug/m^3

   1987–1992, [(0.06 + 1.1 + 0.4)/3] x 1/10 = 0.052 ug/m^3

   1992–1997, [(0.04 + 0.12 + 0.4)/3] x 1/10 = 0.019 ug/m^3

Chapter 8: Conduct Quality Assurance Activities

Once the exposure assessment has been completed, a number of quality assurance activities should be considered. In this section, the two primary types of activities that should be conducted, validation of the exposure assessment and uncertainty analysis, will be discussed.

Validation means different things to different people. To some, it may narrowly mean checking that the calculation routines computed correctly. However, in the following discussion, validation is given a broader meaning. Validation is defined as the process of checking that the results for different workers/jobs and time periods are internally consistent, and that the exposure assessment meets the defined objectives. This may include validation of the accuracy of information transfers from original sources to final study materials (e.g., analysis database). The validation may strive to show that the exposure assessment results reflect the actual study subjects' exposures. This aspect is one that poses many difficulties and is the subject of much research and discussion in the exposure assessment and epidemiology literature.

Uncertainties and variability in an exposure reconstruction always exist. Variability represents a factor that has a known range of values. For example, human body weight is variable, but the range may be known with a good degree of certainty. Uncertainty represents an aspect where the values may not be known, e.g., whether or not a particular worker used a particular chemical. An *uncertainty analysis* seeks to clearly identify the uncertainties, assess their impact on the study, and (possibly) define a strategy to reduce the uncertainties or their effect on the final analysis. The analysis should transparently identify those uncertainties that may be resolved, and those that will likely remain, regardless of the effort put into a resolution plan.

For more discussion on variability and uncertainty, see Morgan and Henrion, 1990 and Paustenbach, 2000 in Attachment A: Essential References.

Validation Approaches

The process of establishing the exposure estimates for the study population introduces professional judgments or assumptions at each step. Therefore, once exposure estimates have been established for each member or group of the study population, some type of *validation* should be completed. This will be easier if you have recorded the decisions and assumptions during the actual exposure assessment work. Criteria for "valid" versus "invalid" should have been defined as part of the study design. For example, "within an order of magnitude" may have been determined to be sufficient. As an alternative, "valid" might mean that an experienced reviewer agrees that the low exposure values are reasonable, as are the middle and high values. There are several ways of gaining important insight into the validity specific assumptions or appropriateness of the entire chain of judgments or assumptions.

A review by Teschke et al., 2002 (see Attachment A) emphasizes validation of exposure assessments for case-control studies, but contains much information of value for other designs.

Expert Panels

Expert panels are a common method for validating the exposure assessment process. These panels usually consist of several (typically, three to five) longtime experts in industrial hygiene either from industries similar to the study population or from research-oriented organizations with experience in retrospective exposure assessment. Each member of the panel may be provided with raw data used to establish the exposure estimates for a small but representative subset of the study population. The panel members may be asked to develop exposure estimates for this subset prior to the panel convening along with a document outlining their judgments and assumptions.

The findings from the expert panel members may be looked at individually or an expert panel meeting may be convened. At the meeting, the original investigator may present his/her exposure estimate and related methods. The panel can discuss the differences in each of their methods with the intent of establishing a consensus. The end result of the process is a list of modifications to the assessment process to improve the overall exposure estimate.

For further discussion of validation using expert panel assessments, see Goldberg, Siematycki, et al., 1986; Fritschi, Nadon, et al., 2003, and Mannetje, Fevotte, et al., 2003 in Attachment A.

Reserved Data

If there is a wealth of exposure data relevant for the operations and time periods, some of that data may be set aside at the beginning of the exposure assessment project. Later, when the exposure assessment is completed, the IH may compare the exposure assessment results obtained to the exposure assessment results using the reserved data. This may not be an ideal approach, since you may be better served using all available the data in the exposure assessment, rather than holding it for the validation.

Indirect Validation — by Study Findings

Some investigators have suggested that since their exposure assessment found a dose-response for the substances and diseases of concern, the exposure assessment is then valid.[37] This may show that the exposure assessment categories were adequately placed with respect to each other, and that study subjects were assigned properly often enough to prevent misclassification from hiding an effect signal. If blinding was not rigorous, and disease cases were differentially assigned to higher exposures, then the positive response findings could be due to the bias. If properly blinded, the exposure assessment may still have significant quantitative error, in that the purported concentrations may all be shifted either high or low compared to the real (and unknown) exposure.

Statistical models developed to predict exposure based on various exposure factors can also be validated. These are sometimes called "cross validation" studies, where for each value. The difference between the prediction and the true value is compared considering significant differences, the confidence intervals, etc.

Biomonitoring Data

In some cases, biomonitoring or medical surveillance data such as blood lead or urinary cadmium levels are available for the specific chemical or substance of interest within a subset of the study population. These data provide a reliable estimate of an individual's dose and can be very helpful in the validation process. However, it is important to remember that biomarkers of exposure represent the sum of total exposure including inhalation, dermal absorption, and ingestion, and do not always directly correlate with air sampling results. Comparing exposure estimates within a specific time period to biomarker data can help validate the process as well as provide important insight into alternate exposure pathways.

Simulated Exposure Experiments

Simulated exposure experiments can also be used to validate assumptions or exposure models used in the exposure assessment process. Conversion factors to normalize sampling data to account for changes in materials, sampling or analysis methods, engineering controls, or work processes over time can be determined by performing controlled experiments. The validity of exposure models can also be tested under controlled conditions. Simulations conducted with the goal of measuring the resulting exposures should pay particular attention to accurately recreating (or accounting for differences) in materials, methods, and environmental conditions compared to the historic period being simulated.

Exposure Assessment Uncertainty Evaluation

Uncertainty in exposure reconstruction may be classified in two categories, scenario uncertainty and parameter uncertainty. Some refer to the scenario uncertainty as "model form uncertainty" since the aspects covered in the model are from the scenario. For further general information, see Appendix A (Morgan and Henrion 1990, and Cullen and Frey 1999). Scenario uncertainty results from missing or incomplete information. This incomplete information can result from errors in grouping workers or job titles, errors in combining exposures from different time periods, or errors in professional judgment. Parameter uncertainty results from measurement or analytical errors and variability in exposure that is not accounted for in the exposure assignments. Parameter uncertainty is usually easier to quantify.

For all exposure reconstructions, whether for an epidemiology study or other purposes, all sources of uncertainty or lack of knowledge regarding the exposure estimate should be documented to establish consistency and transparency, and for identifying the strengths and limitations of the assessment and for allowing an assessment of the uncertainties in the final estimate. This assessment can be a simple process of establishing an exposure range rather than a point estimate. This range is usually established to represent the combined effects of the uncertainties in each judgment or assessment. Uncertainty analysis can also be accomplished by more formal analytical methods such as sensitivity analysis. Yet another approach is via use of confidence scores. Each exposure assessed (individual or groups) could have a confidence score. Then, in the analysis, the epidemiologist could check whether results change by including or excluding data of different confidence.

Developing an understanding of an exposure assessment's uncertainties has long been part of industrial hygiene practice. Typically, this analysis guides decisions on continuing an investigation, proceeding with exposure controls, or concluding that the situation is adequately controlled. Results from uncertainty assessments should be used to determine the benefits of collecting additional information to reduce uncertainty. In addition, the uncertainty of the exposure outlines specific limitations of the final conclusions of any exposure reconstruction.

This section provides a general framework for reviewing the uncertainties in information available for the exposure assessment, including questionnaires and quantitative exposure data. It includes a worksheet for reviewing issues and documenting the reasons behind particular decisions and directions in the exposure assessment.

An "uncertainty analysis" may reflect the main considerations that an experienced industrial hygienist would apply in deciding the next stage to take in improving the exposure assessment. This may or may not lead to additional investigation — other actions may be more relevant, or the IH may have reached the feasible end, where further work could be mostly futile. That is, some uncertainties may be irresolvable. This understanding of the decision factors will support the confidence ratings.

When exposure assessments have significant uncertainty, as most retrospective assessments likely have, an analysis of the nature and impact of the uncertainties should be developed. The analysis will help guide decisions on whether or not to initiate any further investigations to reduce uncertainties.

Initial information review » Uncertainty analysis » Resolution plan » Residual uncertainties » Exposure assessment » Confidence ratings

Inputs to the uncertainty analysis include all available information and the assessment team's knowledge/experience with the operations and exposures involved. This means the information basis may vary in quality and certainty from subject to subject. In some cases, the assessment has meager qualitative information about an operation, and you may have little to no experience with such operations and materials. In other situations, the assessment may have extensive high quality measured exposure data about the operations, and someone that has extensive first-hand experience with such operations has summarized them. The uncertainties and any priorities for resolution may then differ substantially.

Efficient information gathering should resolve the controlling and the most prevalent uncertainties in logical order, with feasibility considering technical aspects, budget, and time as factors.

The Nature of the Uncertainty Affects the Resolution Strategy and Priority

There are a number of sources for uncertainty in an assessment. The uncertainty can shift perceived exposure ... and consequently evaluations of the subject's risk ... either up or down from the "true" risk. The different uncertainties may need different methods for resolution. Air concentration measurements would be a great solution in many cases, but these may not be feasible, and if work history details are lacking, may not resolve the core uncertainties. An optimum approach resolves the main uncertainties before the lesser uncertainties. Which uncertainties are the main ones to resolve first will usually vary from situation to situation. Main categories of uncertainty include:

- Knowledge about the particular operations and materials in the subject's exposure profile. This may be *general* knowledge of the industry or the type of work involved. Or, it may be specific knowledge about the specific worksite, or specific details about what the worker did in his job.
- Background information, from the subject's or co-worker interviews or other records about the materials used, tasks, work methods, or other operations.
- Basis of a quantitative assessment. Generally, measured personal data (M) are better than area samples (A), which in turn may or may not be better than qualitative (Q) assessments. For M and A, the extent of and relevance of past monitoring (including measurements) of the operations must be good. If only very uncertain data is available, an experienced industrial hygienist's Q rating may be more reliable and certain than an M or A would yield in a less experienced IH's assessment.
- Stability of the operations. Operating stability may show high, moderate or low potential for change over time, due to process changes, work method changes, or exposure control changes. Low potential for change operations may need little further consideration, whereas high potential for change situations may need much further investigation, or will result in less confidence in the assessment.
- Variability of the exposures. Exposure profiles that indicate substantial variability from day to day and week to week may cause much uncertainty with respect to average exposure since it is then difficult to estimate typical

conditions. These high variability exposures may require much more monitoring to define exposures than profiles with low variability require.

Uncertainty Analysis

The following list provides categories of potential uncertainties in an exposure assessment. Not all of the items may be relevant for a particular situation. There may also be other factors to consider that are not listed. The industrial hygiene team members responsible for the exposure assessment should use judgment when evaluating the uncertainties in the assessment.

- **Questionnaire "Quality."** If interviews with study subjects or other personnel are used to gather primary study information about the work done, the questions used and the responses given may be a significant source of uncertainty in the project. Evaluating the questionnaire might include such aspects as:
  - Clarity of recall,
  - Consistency of answers, and
  - Agreement with other information about the industry or type of job held.
- **IH Experience.** This is a judgment regarding the industrial hygiene team's skill with the particular operations covered in the work histories and exposure scenarios. Some increase in certainty may be gained via discussion with a more experienced colleague, via "hands on" monitoring, or possibly through further observation in the workplace, or via additional reading of any background on the industry.
- **Measured Exposure Basis.** The quality of the measured data includes such aspects as documentation of the underlying survey strategy, the validity of the sampling and analytical approaches, the relevance of the samples for estimating typical exposures. For a large set of data, statistical analysis may show trends over time that can be used to estimate historical exposures. If the data are limited in number or are not adequately documented with respect to the survey strategy or operations and personnel surveyed, statistical analysis of the data should consider the data's limitations.
- **Qualitative Basis.** Improved modeling or observation, or other improved understanding of exposure potential may be appropriate, as ***may*** exposure monitoring, possibly first via "spot checks." Qualitative assessment certainty may also be affected by the certainties of the factors below.
  - Operations and Task Information. Further discussion with personnel in the operations or further observation may be the productive first step toward resolution of uncertainties. General knowledge of experts or information in publications about the industry.
  - Agent Characteristics. Further review of the physical, chemical, or toxicological properties of the agent may be needed. Monitoring is likely to have little role in resolving this area of uncertainty. Samples (if feasible) of the materials used and subsequent analysis can help. Finding the name of and supplier for previously used materials is important. With that information, the composition information might be found.
  - Workplace Control Reliability. The best approach depends somewhat on what type of control is in use. For example, process containment may be verified by methods other than exposure monitoring.
  - Assessment Group Composition. Either further discussion with knowledgeable personnel about work assignments or much more monitoring may be used to resolve the group composition.

The approach to the uncertainty evaluation depends somewhat on the EA design and its goals. The purpose of the following framework is simply to illustrate the possibilities. These may not fit all projects, and other rules or revisions to these may be more appropriate.

Example of Exposure Assessment Uncertainty Evaluation for Scenario 1 — Beryllium

This chapter will also consider the beryllium example discussed in previous chapters. The first information on exposures and work histories come from two sources. For exposure, the IH finds a general summary report, reading as follows. "For the 111 beryllium in air samples available for 1982 to 2007, the average is 0.9, the median 0.12, the minimum 0.002 and the maximum 50 mg/m^3." For work histories, the only listing is the "last job held" and a date retired or last date of employment if otherwise no longer working at the facility. This information is from a human resources payroll system.

Exhibit 8.1 — Exposure Assessment Uncertainty Evaluation

Industrial Hygiene Expert Experience	
Good	Multiple years of measurement survey experience in facilities and with agents like the operations assessed
Fair	Some years of measurement survey experience in operations that have some similarities (materials or processes) to Limited experience with operations that have limited similarities of processes or materials.
Poor	Limited (< 1 year) experience or no experience with operations or agents with any similarities to those assessed.
Assessment Basis	
a. Measured (M) Personal Exposure Data, Area (A) Exposure Data	
Good	Multiple, well-documented, reports of the agents and operations assessed, with statistical analysis. Routine monitoring established. Covers relevant time periods.
Fair	At least one survey completed and documented, for relevant workers, work activities and agents. Some recent, relevant area monitoring data, or limited spot measurements of concentrations in the work area; little to no information on their rationale. The relevance of the data to the time period of interest is based on suggestions that the operations have been relatively stable (no major changes in production technology or in control measures).
Poor	No data for the operations and agents assessed, or data is from time periods for which relevance cannot be established, or only poorly described, broad summary data are available.
b. Qualitative Basis	
Fair	By analogy to same operation somewhere else or by worst case modeling and results show low to no exposure potential. By other proven models. By comparison to somewhat similar operations and agents for which good data is available.
Poor	No information or modeling available for the operations and agents assessed
Extent of Operations and Task Information	
Good	Detailed interviews with multiple workers from the operations who understand the questions. Walk-through review of main tasks and work methods.
Fair	In-person interviews with at least one worker, at least a walk-through of the facility assessed to telephone discussion of some points, at least a familiarity with the operations via a past tour of a similar facility
Poor	No discussions, no review of the facility
Questionnaire "Quality" — General Aspects	
Good	Respondent subject was generally mentally alert and exhibited good recall of most questions.
Poor	Respondent was confused or for other reasons could not answer many questions.
Questionnaire "Quality" — Job Knowledge	
Good	The respondent subject could state with confidence that his job DID NOT involve exposures of concern from the study list and worked in an industry for which this is reasonable The respondent worked only as a manager in an industry of concern and reports no exposures of concern The respondent could state with confidence that his job DID involve at least one of the study exposures of concern and worked in an industry for which this is reasonable
Fair	The respondent worked in an industry unlikely to have exposures of concern and states he was exposed to "X" with a good explanation
Poor	The respondent worked in an industry that may have had exposures of concern as a general worker but could not describe the chemicals worked with.
Factory, Worksite Information	
Good	The study database or other reliable information (e.g., worksite inspection) shows exposures of concern at the worker's employer and the worker held a job with probable exposure. The study database or other reliable information shows the worker's employer DID NOT have exposures of concern and this is reasonable for the industry. The history of the location gathered during an inspection shows reliable information (multiple people, or purchasing records, or engineering records) that the employer had exposures of concern in the past in periods relevant to the employee.
Poor	Little to no reliable information is available about the nature of the operations and exposure potential at the factory.

Joe Smith. Machinist. Retired 31 January 1995
Samuel Adams. Welder. Retired 30 June 1996
Phil Jones. Supervisor. Retired August 15 1997

From discussions with current workers, it is discovered that the machinists all worked with beryllium alloys, but some more than others. The welders had a few that did all of the welding for the beryllium alloys, but other welders handled only other materials. Currently, supervisors do not do any hands on manufacturing work. What might the IH conclude from a preliminary uncertainty analysis?

Exposure Data. The summary is rated as poor. The survey strategy cannot be determined, as well as whether these are short term or full shift samples, etc. This establishes a priority to search further for more detailed exposure survey reports.

Work Histories. This is rated this as fair. The final job titles and date of retirement are known. However, the IH needs to find out which of the welding categories Sam Adams held, and what supervisors did in earlier years.

If the IH can do no further investigation, how might they handle this data, using confidence scores? On an Exposed, Unexposed scale:

Joe Smith, exposed, high confidence
Sam Adams, exposed, low confidence
Phil Jones, unexposed, low confidence.

In the epidemiologic analyses, these scores could be used to test how results change by selectively including or excluding groups with high, moderate, or low exposure confidence.

As often happens, these ratings are quite arguable, and all would agree further investigation should be conducted to resolve the uncertainties. Since it is known that beryllium exposure is hazardous, an exposed, unexposed exposure assessment does not contribute quantitative knowledge about beryllium. Therefore, a further goal would be to find sufficient information to derive reliable quantitative or semi-quantitative exposure estimates.

After further investigation, the IH finds additionally informative materials. The human resource department has records that give more details in personnel files. In addition, they find a more detailed summary of the original industrial hygiene survey reports from which the management summary was prepared. It is also discovered that the usual sampling was for 15 minute periods during typical task operations.

Samuel Adams. Welder, Assigned to beryllium alloy section, 1982 to retirement.
Phil Jones. Foreman and vacation fill-in, general machining.

The IH evaluates again and rate the exposure data as fair. They would like to know more about the distribution of the data, and further verify that the samples were for 15 minutes in typical conditions. The IH would also like to know the sampling and analytical methods used, air sampling calibration practices, and the qualifications of the analytical laboratory. You evaluate the work history for Sam as good, and for Phil as fair. They would also like to know more about what Phil did and how much time he spent on the production tasks. In a telephone interview, Phil (alive and well) states that he did about 70% administrative work, with the remainder spread over shaping, grinding, and polishing in about equal portions. His work history is now rated as good. Since the interview approach worked, the IH also interviews several machinists about their work in the past. During the first round of this, Joe was not available, but other machinists interviewed state that Joe specialized in working with the beryllium alloys, performing a mix of all the machinist tasks. Since the information is consistent from multiple sources, a high confidence score is assigned to the work history part of his exposure assessment evaluation.

In some cases, a more formal uncertainty assessment may be necessary. For example, consider that an exposure assessment has just been

Note: Hypothetical Data for This Example (not from any real beryllium samples) in mg/m^3

Task	*2002–2007*	*1997–2002*	*1992–1997*	*1987–1992*	*1982–1987*
Shaping	N=10 AM= 0.02	N=10 AM= 0.03	N=6 AM= 0.04	N=4 AM= 0.06	N=3 AM= 0.09
Grinding	N=12 AM=0.15	N=4 AM=0.6	N=7 AM=0.12	N=0	N=2 AM = 2
Threading	N=3 AM= < 0.002	N=0	N=0	N=0	N=3 AM= 0.005
Welding	N=5 AM=0.02	N=5 AM=0.05	N=5 AM=0.1	N=5 AM=0.2	N=5 AM=0.2

completed at A Bicycle Company (ABC) involving assignment of cumulative exposures for all current and former employees. The manager at the IH's consulting firm wants to make sure the interpretation of the data that is presented to ABC is as complete and accurate as possible. He asks that you perform a basic uncertainty analysis to determine whether additional data should be collected before presenting the analysis to company management. He outlines the following objectives:

1. Determine the effect of exposure uncertainty on the association the IH is seeing between high beryllium exposure and chronic beryllium disease.
2. Identify the opportunities for data supplementation that will have the greatest effect on reducing uncertainty.

Luckily, being the plan-ahead type, the industrial hygienist anticipated this question at the outset of the project. He or she meticulously documented their data with confidence ratings at each major step using a scale of 3=Good, 2=Fair, 1=Poor, and 0=No information. These confidence ratings were applied to job assignments and beryllium exposure data. Using this numerical scale, an average confidence rating could be calculated for each individual's overall work history and each individual's cumulative exposure, allowing separate evaluations of the contributions of work history and exposure data to uncertainty. These ratings and calculations were applied in the following manner:

- Job Assignments Confidence Ratings (JACR) were established for each job assignment in an individual's work history. A "Good" rating indicated that there was clear documentation or multiple corroborating sources describing the start and end dates of the job assignment, the tasks involved in the job assignment, and the approximate percentage of time spent working with beryllium. A "Poor" rating indicated sketchy documentation, only approximate start and end dates, and conflicting reports of the percentage of time spent working with beryllium.
- Average Job History Confidence Ratings for each individual were calculated as the sum of all the JACRs multiplied by the number of years at the job assignment divided by the total years worked at the facility. This calculation results in a scaled average weighted by the amount of time spent at each job assignment. For example, Fred worked at ABC for 10 years in three different jobs. He worked in job one for 3 years with a JACR of 3, job two for 6 years with a JACR of 2, and job three for 1 year with a JACR of 1. His overall JACR would be (3 x 3/10) + (2 x 6/10) + (1 x 1/10) = 2.2 which puts him in the "Fair" to "Good" range.
- Exposure Confidence Ratings (ECR) were established for each defined interval for each beryllium process. A rating of "Good" indicated at least 10 representative, non-biased beryllium measurements for the given task or process. A "Poor" rating indicated at least 1 beryllium sample from the given task and time period.
- Average Exposure Confidence Ratings were also calculated for each individual using the same weighted average method as for the total job history confidence ratings.
- The Overall Cumulative Exposure Confidence rating was calculated as the average of the Average Job History Confidence Rating and the Average Exposure Confidence Rating.

As all the data has already been collected, achieving the objectives set by the IH's manager only requires a little extra number crunching. The first step should be to determine how the risk of beryllium disease (as determined by the chosen epidemiological model) changes depending on the uncertainty or confidence rating of the exposure assessment. This involves creating subsets of data varying by confidence rating. For example, given the median Average Job History Confidence Rating for all employees was 2.1, a subset of data containing only employees with an Average Job History Confidence Ratings less than 2.1 was created to evaluate the effect of uncertainty in job histories. This process was repeated three times to determine the effect of uncertainty in the job history, the beryllium exposure ratings, and the combined effect of the two. The table below shows the results of this evaluation.

Table 8.1 — Odds ratios for developing chronic beryllium disease (increase in risk per unit increase in exposure) by subset of data (sample data only)

Data Included	*Odds Ratio*
All Data	1.3
Only Average Job History Confidence Ratings > median	1.6
Only Average Exposure Confidence Ratings > median	1.0
Only Overall Cumulative Exposure Confidence Ratings > median	0.9

Generally when looking at the effects on odds ratios with different subsets of data, it is important to inspect both the odds ratio and the confidence interval for the odds ratio. However, for the sake of simplicity, we will only examine a point estimate of the odds ratio in this example. Based on Table 8.1,

it appears that only utilizing individuals with "Moderate" to "Good" Job History Confidence Ratings results in an increase of more than 20% in the odds ratio for beryllium exposure. This suggests that misclassification of exposure due to poor quality job history records attenuates the observed dose response. The results of the other two subset analyses indicate a more than 20% reduction in the odds ratio when only high quality exposure records are used. It is more difficult to determine the exact cause of this attenuation. However, upon closer inspection of the records of the individuals represented in these subsets, it is observed that the range of exposures has been greatly reduced compared to the complete data set and may not represent a large enough range to test the effects of beryllium exposure.

Based on this analysis the IH reports back to his or her manager that misclassification of exposure from job history quality problems is reducing the reported effect of exposure, which is likely not a big problem. In addition, they report that the effect of low quality exposure data is unclear, but when only using exposure data rated as "high quality" increases in beryllium exposure do not correlate with increases in chronic beryllium disease. This may present a significant problem, and more data should be collected.

In order to determine the best use of resources in collecting additional data, the IH decides to compile Table 8.2 which shows the Exposure Confidence Rating and the number of individuals who have ever been assigned to each job in each time period. Based on this table, it is clear that data from 1982–1992 in grinding would greatly increase the confidence level in the assigned exposures since these cells have low confidence ratings and large numbers of employees. More data from Polishing in 1982–1987 might also be beneficial. Based on these observations, the IH recommends to his or her manager that more information is needed on grinding exposures from 1982 to 1992. This may require additional employee interviews, literature searching, and/or simulation studies to supplement the existing data.

Table 8.2 — Exposure Confidence Ratings and number of employees (N) ever assigned to task by time period

Task	*2002–2007*	*1997–2002*	*1992–1997*	*1987–1992*	*1982–1987*
Shaping	Good N=25	Good N=32	Moderate N=23	Moderate N=19	Moderate N=8
Grinding	Good N=50	Moderate N=54	Moderate N=48	No Information N=37	Poor N=12
Threading	Poor N=4	No Information N=5	No Information N=3	No Information N=2	Poor N=1
Welding	Moderate N=8	Moderate N=11	Moderate N=7	Moderate N=5	Moderate N=3
Polishing	Moderate N=18	Moderate N=25	Moderate N=21	Moderate N=16	Poor N=11

Chapter 9: Maintain Exposure Assessment Documentation

Numerous documents and other types of information will be gathered in the process of conducting a retrospective exposure assessment. It is important to organize and maintain sufficient information for the individual IH's report writing, as well as for others to follow and verify the work, or to build on it in subsequent studies. Documents to maintained, as available, include (see Chapter 5 for details of the documentation that fall into each category).

- Literature and any notes from conversations with experts in the field gathered as part of the initial research and planning
- Basic Workplace Characterization Documentation
- Workforce Characterization Documentation
- Exposure Group Documentation
- Exposure Assessment Documentation
- Reports or Publications Prepared as Part of the Study

Exposure Recordkeeping for Future Uses

Once you have worked through the process (and obstacles) of reconstructing exposure from typically limited and scattered information, you will appreciate the relevance and importance of recordkeeping in anticipation of future long-term data needs a need. As a practicing IH, you have control over collection of exposure information used to address current and future questions. However, you do not know what future questions may be asked.

How does an IH go about documenting for future data needs?

Because of the long-term focus on individual and similar group exposures, the classical approach of having documentation revolve around the sampling event is not efficient or effective. However with very little modification, the practicing IH can maintain records that serve both current and future data needs. In order to conduct future exposure assessments, there should be documentation to characterize both the workplace and workforce for each exposure group.

The vast majority of all exposure scenarios will not be measured for many reasons including resources (people and money) and low assessment of risk. But each exposure scenario does need to be listed and classified into at least a range of exposure. This is best accomplished by the practicing IH today through a combination of deterministic modeling, chemical and physical property data modeling, known expected performance of engineering controls, and professional judgment.

With this approach, the pertinent information associated with working in a particular exposure group is compiled once. An estimate of how much time a worker spends in particular exposure groups is either collected on an ongoing basis or on a periodic basis such as semi-annually or annually. It is normal for a worker to spend time in multiple exposure groups even over very short periods of time such as a day or week. The documentation associated with any specific exposure group is applicable to each individual who works in the exposure group.

If a worker has not worked in an exposure group that contains the agent(s) of interest, it is known that they were not exposed. If they worked in an exposure group where an agent was listed and not monitored, the future researcher will have an estimate of exposure based on the first hand knowledge of the IH at the time of the exposure. Additionally, if there is quantitative data, estimates for the individual could still be obtained. Finally this approach addresses the problem that individuals may be exposed to the same agent but in multiple exposure groups. Here an exposure assessment is developed for each exposure scenario which can then be added across all scenarios.

Although this effort appears significant, it is much less time consuming than is sampling every exposure and is much less expensive. Further, an exposure assessment exists even in the absence of sampling.

What types of metrics are needed for long-term data needs?

For compliance purposes, the geometric or arithmetic mean and standard deviation of an eight-hour time-weighted average are appropriate and useful metrics. Because disease may be associated with different exposure metrics, such as daily or weekly average, long term average, number of peak exposures per

day, week, or month above some level, cumulative exposure, etc., simply knowing that the PEL or other OEL is not exceeded may not be useful for such studies. Thus the practicing IH should retain as many statistics as possible that help to describe the exposure distribution. A portion of the exposure scenarios that have been classified into exposure ranges should be evaluated with quantitative data to assess the accuracy and validity of the classification methodology. The documentation of these evaluations should be maintained.

Other recordkeeping considerations for long-term data

The documentation listed above and in Chapter 5 is all suggested as good recordkeeping for practicing IHs. It has been shown that this same information is needed to reconstruct exposure properly in the future. However, often many of these data elements are missing from the historical records.

- Some critical data may never have been recorded. In particular, future exposure assessors often do not have the following information available:
  - The reason and strategy for sampling. Is it to assess compliance? If so, is worst-case being monitored? Is it to assess a change in controls? If so, what was the change?
  - Lists of specific workers who are included in a given sampling event, (i.e., all the SEG members, preferably by name). Generally, only the worker(s) who actually wore the pump are listed on the sampling log.
  - Similarly, because work without anticipated exposure is not monitored, there is seldom a list of workers without exposure. It must often be assumed by job title or lack of information that a worker (or group of workers) had no exposure.
  - Types of sampling event data often missing include the sampling methodology, controls in place at the time of sampling, and actual exposure time (as compared to sample time). This may be because the IH is familiar with existing conditions and does not feel any need to record them.
  - Other types of data often missing include a history of changes in controls and the frequency of peak exposures. Again, such data may not be recorded because it is a known fact at the time.
- Often data is lost or widely dispersed. In a large company, reports may be archived to save space in work areas. When a company is sold, hard-copy records may be sent from the facility to the new headquarters, where they may be stored or disposed. Use of electronic databases to record exposure data can help with this type of missing data.
- Critical exposure data may be located in several documents, making it difficult to find and tie together, especially if dispersed. For example, a discussion of why exposure monitoring was done and existing controls may be in a text-based exposure report, while the method and duration of sampling, limits of detection, and date of sample collection may be on sample logs or laboratory reports. SEGs may be delineated in another document, perhaps in an overall exposure assessment strategy. While the full text from exposure assessment reports is difficult to insert into an electronic database, key data elements can be abstracted into the database. In addition, links to or a listing of related documents can be included in the database.

Practicing IHs should look at the exposure data they collect today and imagine someone else trying to interpret the same information 5, 10, or 20 years later to determine what was actually going on when now-ill workers were still healthy and being exposed. When it is clear that some additional information would be useful in such a future dose reconstruction effort, the industrial hygienist should attempt to include that information in the current records.

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Attachment B: Glossary

**Words in the glossary are italicized in the text where defined or on first use.

Bias – The alteration of true data values as a result of random or systematic errors.

Case-control study – A type of epidemiological study that estimates the risk for an outcome using a comparison of risk factors and exposure experienced by those with the outcome (cases) and those without the outcome (controls). Case control studies are always retrospective.

Case-to-control ratio – the number of controls per case in a case-control study.

Case prevalence – The proportion of cases of an outcome within a population at any time.

Coding – A systematic categorization of data.

Cohort study – An epidemiologic study that compares the risk for a specific outcome in an expose population with an almost identical unexposed population. Cohort studies can be retrospective or prospective.

Co-morbid risk factors – Behavioral or genetic risk factors that change the susceptibility of a study participant to the effects of the exposure under study. These are considered to be effect modifiers.

Confounder – A risk factor that is associated with the study outcome and exposure, causing the true contribution for the risk of the outcome due to exposure to be obscured. For example, if you are studying the risk of lung cancer due to welding fume, you must consider smoking to be a confounder because smoking is more prevalent in people who weld and is a risk factor for lung cancer without exposure to welding fume.

Data collection protocol – The objectives and specific procedures to be used in the collection process.

Disease – Any adverse health outcome including mortality and injury.

Disease cluster – An unexpected number of cases of the same disease that share the same exposures during a relatively short period of time. If the exposure is environmental, then the cases share the same relative geographic location. If the exposure is occupational, then location is not as important as a shared exposure to a specific chemical or operation.

Effect modifier – A factor that is does not have an equal effect across the strata of a study. This could be due to genetics, hormonal status, gender, or age.

Epidemiology – the study of epidemics (broadly including diseases, illnesses, and injuries) and the associated causes and risk factors.

Exposure metric – The unit of exposure assigned to study participants.

Healthy worker effect – A type of bias that can be introduced into a study because workers that survive, i.e. work for several years, are less likely to suffer from adverse outcomes than those who do not work. Those affected most by the study exposure are more likely to leave the job early or acquire disease earlier, skewing the dose response curve.

Hypothesis – The question a study seeks to answer.

Information bias – The bias introduced into a study due to the way information is collected, analyzed, or interpreted.

Job dictionary – A list of jobs, job titles, or other occupational classification with associated job tasks and exposures.

Job exposure matrix (JEM) – A tool used to assign measures of exposure to each study member based on selected indices (e.g., job title, chronological year, and task). When task is included in the JEM, it may be referred to as a task-based exposure matrix (TEM).

Latency Period – The time from disease initiation to disease detection.

Occupational exposure – Contact between a subject and a particular agent in the workplace, assuming that contact occurs when a person spends time in a work environment in which the agent is present, resulting in at least some uptake of the agent into the body through one or more routes of exposure.

Occupational exposure reconstruction – the process constructing past workplace exposures from existing data, interviews with workers, and professional judgment.

Recall bias – The bias introduced into a study due to the preferential recall of study members based on their exposure history. People who were exposed to an agent and have an illness are more likely to recall their work history differently than those who were exposed but are disease free.

Retrospective exposure assessment – Assessment of workplace exposure conducted after a disease or illness has been identified or reported, or in the case of medical surveillance or risk assessment, after the opportunity to collect additional exposure measurements have passed.

Sampling bias – The bias introduced into a study due to preferential sampling of workers with suspected high exposure and using that exposure intensity for all workers in that job. Randomly sampling workers or systematically adjusting the exposure intensity for those less exposed can reduce sampling bias.

Selection bias – The bias introduced into a study due to preferential selection of study members.

Sensitivity analysis – The testing of an exposure model using real or simulated data to determine the model robustness. Withholding some data from the model development phase and using it to test the model can accomplish this.

Similar Exposure Group (SEG) – A group of workers having the same general exposure profile for the agent(s) being studied because of the similarity and frequency of the tasks they perform, the materials and processes with which they work, and the similarity of the way they perform the tasks.

Study power – The number of cases and controls or cohort members required to detect an effect if it were truly present based on assumptions about prevalence of the outcome in the unexposed population and the level of significance.

Uncertainty analysis – The process to clearly identify the uncertainties, assess their impact on the study, and (possibly) define a strategy to reduce the uncertainties or their effect on the final analysis.

Validation – The process for checking that the results for different workers/jobs and time periods are internally consistent, and that the exposure assessment meets the defined objectives.

Attachment C:
Work Site Investigation Checklist for Exposure Reconstruction

The goal of a work site investigation for exposure reconstruction is to gather information about current and past operations where the study subject(s) worked. One part of the investigation is to find current and past exposure information. The investigation also seeks information on the dates and types of changes that may have altered exposure in the past. This may include changes to the:

- workplace layout or production process,
- composition or quantity of materials used or produced,
- tasks and work practices used by the subject, and
- controls used currently and in the past to reduce the worker exposure to workplace hazards.

The investigation should focus on jobs and work areas relevant to the study subject(s)' work history.

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This checklist is provided to guide the work site investigation. Each item on the checklist should be considered and where relevant information is found, it should be recorded. Because each work site will present different aspects to review and record, the inspection team will need to use judgment on what parts of this checklist is relevant a particular work site and study objectives. Section 1. Subject and Work Site Identification may be held off until the inspection team has gained a preliminary knowledge of the nature of the operations at the work site and of the subjects' work. [General published references may also provide some preliminary information about the work and possible exposures.] After an initial and quick review of the work place, some aspects of the inspection can rapidly be eliminated, and others focused on in more detail.

First, be sure and record basic information about the investigation.

- ❑ Name and contact information for person(s) completing the work site investigation
- ❑ Date(s) of work site inspection
- ❑ List exposure(s) of concern
- ❑ List Industrial hygiene survey and sampling report(s) tied to this investigation
- ❑ Overall comments about the investigation — limitations
- ❑ Type of investigation: preliminary (first visit), final investigation

1. SUBJECT AND WORK SITE IDENTIFICATION

- ❑ Study Subject(s) ID Number(s)
- ❑ Work Site ID Number or Description, Address
- ❑ Relation of site to where the subject worked (same or different — if different, describe procedure was followed to establish equivalence)
- ❑ Personnel at Facility Contacted — name and contact information
- ❑ Relevant dates for each job at this work site from the subject(s)' interview questionnaire
- ❑ Area of the facility where the subject worked for each job 1
  - ❑ Records to confirm location information — personnel, payroll, or medical records

1.1. Initial Work Site Review

- ❑ Based on a short discussion and inspection, indicate whether facility has potential for current exposures of concern or possible past exposures of concern

  Following a brief discussion with work site personnel and a quick inspection of the work site, it will be possible to decide to a) continue or b) end the inspection. Ending it is possible if there is no current or past potential for exposures of concern due to the nature of the work done and the types of materials used.

2. TASK INFORMATION

Look for information on all tasks with current or past potential for exposures of concern relevant to the scope of the study. Information about how PAST tasks were different is especially important. Tasks are the activities that are part of the overall job. For example, for the job painter, tasks might include a) preparing surfaces, b) mixing paints, c) applying paints, and d) cleanup of equipment. Information about such tasks' duration and frequency will help better understand the typical exposure and the exposure variability. The frequency and duration information can also help in estimation of average exposures from the measured data for specific tasks or from specific work areas where main tasks are performed.

- ❑ Each task involving USE or CONTACT with exposures of Concern
- ❑ Agents used or contacted in each task
- ❑ The Frequency of exposure to each agent used or contacted in the task (Average or Low, Mid, High, and # times per day, week, month, year)
- ❑ The Duration of exposure to each agent used or contacted in the task (Average or Low, Mid, High and # minutes, hours, days per day, week, month, year)

  * These and all subsequent, similar responses may be given as either an estimated average or as a range. If as a range, please try to report the low, typical and high ends of the range.

3. TASK CHANGES OVER TIME

The focus is on any changes that altered the opportunity for exposures of concern. Changes in the types of tasks, their duration or frequency, or the equipment and materials used are all of interest. Did any of the following aspects of the tasks that are part of the subject's job change over the time period of the subject's employment?

- ❑ Type of tasks (If yes, when (year) did the change occur? Describe the change)
- ❑ Frequency of tasks involving exposure to materials of concern (If yes, when (year) did the change occur? Describe the change)
- ❑ Duration (minutes or hours) of tasks involving exposure to materials of concern (If yes, when (year) did the change occur? Describe the change)
- ❑ Materials used (If yes, when (year) did the change occur? Describe the change)

4. INDIVIDUAL WORK PRACTICES & CONSISTENCY/DIVERSITY OF WORK METHODS

- ❑ For each task, note whether the tasks were of a sort where the way an individual does the work will affect the exposure to a significant extent. Consider such aspects as body position, spilling of materials.

  As an example, any tasks that involve the manual handling of materials in buckets or other open containers can involve different amounts of spillage that depends on how careful the individual might be. Dumping bags of powdered material into a reactor could also be affected a lot by individual work practices, such as how quickly the worker opens the bag and dumps it, and by how much and how long the worker shakes the bag to empty it.

5. EXPOSURE MEASUREMENT RECORDS

You need to understand as much as possible about the when, where, how, and why behind exposure measurements. Without the details, it is not known what the results represent and it will be difficult to use them to estimate exposures. Obtain and attach copies of the relevant monitoring records when possible!

- ❑ Summarize any site maintained exposure monitoring data relevant to the jobs, specific tasks, and work area.
- ❑ Basis for monitoring
  - ❑ Personal sampling — Short term for specific activities, Representative of the full work shift, or Do not know
  - ❑ Breathing zone area samples at work stations
  - ❑ Source samples to define contaminant points of origin
- ❑ Operating conditions like when the measurements were taken — typical or usual operations, unusually contaminated (upset) conditions, low or high production period, or unknown
- ❑ Years covered in the monitoring records
- ❑ Prior monitoring methods and years used (Note: a conversion factor may need to be developed)
- ❑ Subject's work areas or tasks for each job covered by the monitoring records
- ❑ Other chemicals or other exposures (e.g., ionizing radiation) included in the exposures monitoring records

6. NEW ON-SITE MEASUREMENTS

- ❑ Results of any direct-reading analysis or other monitoring results conducted during the work site investigation. Relate these to the subject's work locations and tasks. Sketch the workplace and sampling locations.

7. WORKER RECORDS — PERSONNEL RECORDS

Some factories may keep a variety of records that can help understand the work. The goal here is to ask about any records that cover what the study subject did at the factory. Do records exist about what chemicals were used, or where the materials were purchased? If yes, these records might tell us something about the quantity used or about the material's composition. However, this section is just about the personnel records. If records do not exist, interviews with personnel from those areas who know the production process well may provide these estimates.

- ❑ Source of work history information (Site personnel records or interviews) — verify the

hire date, date left job (retired or other reasons), dates of changes in jobs held
  - ❑ typical hours worked per day
  - ❑ Days worked per week _____
  - ❑ lunch break and other break periods # per day
  - ❑ # holidays per year _____
  - ❑ vacation periods (days per year) _____
- ❑ Estimate of how much time the subject(s) spent in each area for current and past exposure periods. A range estimate may be provided.

8. WORKPLACE LAYOUT AND PROCESS INFORMATION

Some work sites will be very simple in layout and with very simple production methods. A shoe factory is pretty simple. A petroleum refinery is pretty complex. But, we are interested only in the parts of the work site where the study subject(s) worked. This may be just one or it might be several parts of a complex site.

- ❑ Provide diagrams or photos of the relevant work areas where possible.
- ❑ Basis for workplace layout and process information
  - ❑ written records — describe types
  - ❑ Interviews — provide names and job titles
- ❑ Current production level (Steady production (about the same from day to day), Cyclic (describe cycle), Seasonally different (describe), Different in an unpredictable or random manner (describe)
- ❑ Past production level (Steady production (about the same from day to day), Cyclic (describe cycle), Seasonally different (describe), Different in an unpredictable or random manner (describe)
- ❑ Dates and nature of major changes to process and production methods — capacity, process or work flow, changes to the process such as process pressure, temperature, or containment
- ❑ Changes to the layout of relevant workrooms or buildings (increase or decrease in the number of machines or other equipment per square meter, size or capacity of machines or other equipment per square meter, number of workers per square meter of floor space, or quantity produced per worker assigned)
- ❑ Changes in the distances or direction between the work station for the subject and air contaminant sources in the work area (describe)
- ❑ Dates of each change

9. BREAK AREAS

You want to try to account for all the hours in the subject's typical work day, and where those hours were spent. Some work sites had no special rooms for smoking or tea breaks, or for lunch.

- ❑ Locations where the workers spent their break time including lunch (work station, break room, lunch room away from the work area, someplace else (describe))
- ❑ Ventilation and cleanliness of break areas

10. MATERIALS OF CONCERN USED OR PRODUCED

Provide details on chemicals, solvents, and other materials used in and produced in relevant work areas and jobs that contribute to the exposure of concern. The minor quantities and infrequent, short uses with little exposure potential are of less interest than are the larger quantities and more frequent uses and higher exposure potential. Estimated ranges are OK, but whenever possible, a most likely value will be much better. Use chemical names where possible or code letters that can be linked to the chemical. Sometimes, trade names or brand names may be all that is available. Obtain samples of "suspicious" materials if possible, for analysis of content of chemicals of concern. This should cover jobs most similar to that previously done by the study subject. The goal is to quantitatively assess exposure potential to the agent(s) of main concern, and assess presence or absence of the other exposures (chemicals, radiation, etc) of concern.

- ❑ List chemical or materials currently used
- ❑ If not a pure substance, percent by weight/volume of exposures of concern
- ❑ Frequency of usage of each chemical or material (daily or __ times per week, month, or year)
- ❑ Quantity used in work area (___ mL, liters, grams, kg, or metric tons per day, week, month, year, other). May be as a range.
- ❑ Duration (minutes or hours per day, week, month, year) of use

11. PAST USE OF MATERIALS OF CONCERN

Getting this information is even more of a challenge. If the past use was about the same as the present, make note of that. But, if the past operations seem to have differed substantially from the current situation, this section is very important. Check if any analytical data exist with regard to the composition of materials used or produced in the past. If good relevant exposure monitoring records exist for the relevant past periods, this section becomes much less important. In

such cases, the exposure data will be the primary method for estimating exposures.

- ❑ List chemical or materials used in the past and the dates of use
- ❑ If not a pure substance, percent by weight/volume of exposures of concern
- ❑ Frequency of usage of each chemical or material (daily or __ times per week, month, or year)
- ❑ Quantity used in work area (___ mL, liters, grams, kg, or metric tons per day, week, month, year, other). May be as a range.
- ❑ Duration (minutes or hours per day, week, month, year) of use

12. EXPOSURE CONTROLS USED

Current and prior controls) will help you relate any current exposure data to prior conditions when controls may have differed. If current and past exposure monitoring data exist, the information on controls will help in interpreting the data and improving the estimated past exposures.

- ❑ Blueprints, drawings or photographs that give a historic perspective on the facility and its operations. Obtain copies when possible (note that photographs of such items may be considered).
- ❑ Current Controls
  - ❑ containment
    - ❑ full enclosure, continuous process
    - ❑ full enclosure, continuous process except for sampling, introduction of process additives
    - ❑ enclosed, batch process but open for start or end of production run
    - ❑ partial enclosure of process(describe)
    - ❑ open system — no enclosure
  - ❑ ventilation (see following section)
  - ❑ chemical protective clothing
  - ❑ respirators
  - ❑ substitution, elimination
  - ❑ separation by distance
  - ❑ administrative or worker rotation
  - ❑ other (describe)
- ❑ Prior Controls (if different from current operations. Note the estimated year of any of key changes.)
  - ❑ containment
    - ❑ full enclosure, continuous process
    - ❑ full enclosure, continuous process except for sampling, introduction of process additives
    - ❑ enclosed, batch process but open for start or end of production run
    - ❑ partial enclosure of process (describe)
    - ❑ open system — no enclosure
  - ❑ ventilation (see following section)
  - ❑ chemical protective clothing
  - ❑ respirators
  - ❑ substitution, elimination
  - ❑ separation by distance
  - ❑ administrative or worker rotation
  - ❑ other (describe)

If an exhaust ventilation system is now in use, it may be possible to evaluate conditions with the system on and also with the system off. With the system off, you may gain insights into exposures prior to the system's installation. If this "system off" evaluation is undertaken, adequate temporary protective measures must be in place. Direct reading instrument readings under both conditions may give insights into the ventilation effectiveness.

- ❑ Current Ventilation
  - ❑ An open window or open windows
  - ❑ A fan in the window or windows
  - ❑ A fan or fans on the floor
  - ❑ Fume hood with fan and air filters or with a waterfall
  - ❑ Exhaust system with a hood overhead where you worked
  - ❑ Exhaust system that captured material close to source
  - ❑ A walk in booth with a mechanical fan
  - ❑ A closed room with a booth on one end
  - ❑ No special ventilation
  - ❑ Other (DESCRIBE)
- ❑ Past Ventilation (if different from current operations. Note the estimated year of any of key changes.)
  - ❑ An open window or open windows
  - ❑ A fan in the window or windows
  - ❑ A fan or fans on the floor
  - ❑ Fume hood with fan and air filters or with a waterfall
  - ❑ Exhaust system with a hood overhead where you worked
  - ❑ Exhaust system that captured material close to source
  - ❑ A walk in booth with a mechanical fan
  - ❑ A closed room with a booth on one end
  - ❑ No special ventilation
  - ❑ Other (DESCRIBE)
- ❑ Quantitative or qualitative description of the extent of the change on exhaust air from the work area for each ventilation change (fan capacity, system well designed, adequately maintained)

13. DERMAL EXPOSURE POTENTIAL

If there is no potential for "significant" skin contact, this section is not important and should be skipped. Usually, significant skin contact carries with it significant inhalation exposure. If workers have a good exhaust ventilation system, but have hand contact with solvents, the skin contact might then be significant, even though inhalation exposure is small.

- ❑ List of chemicals of concern that subject(s) got on hands or other parts of body
- ❑ Frequency that subject(s) have chemicals on hands or other parts of body (Never, Sometimes, Do not know OR # Times _____ per day, week, month, year)
- ❑ Extent of skin coverage (finger, fingers, one hand, both hands, arm and hand, arms and hands, more than hands and arms (describe))
- ❑ Duration chemicals were on hands before washed off (minutes, hours, days, at lunch time, at lunch and end of day, don't know). May be provided as a range.
- ❑ Product used to clean hands (Commercial hand cleaner or soap, Gasoline, Mineral oil, Mineral Spirits (Naphtha), Something else (SPECIFY _____)

14. MEDICAL RECORDS

Medical records may seldom be available at any but medium to large factory sites. If such records are available, they may provide some useful details about the individual's work, medical and exposure history. Review when possible and summarize relevant information from the records. Note that these records may be confidential or other wise privileged and informed consent procedures may be required for access. Regulations may apply to this aspect.

- ❑ Biologic monitoring records
- ❑ Significant exposure event records
- ❑ Compensable disease records
- ❑ Non-workplace exposures, confounders (smoking, alcohol, diet, hobbies, secondary work)
- ❑ Medications, "medical" events (i.e., major illnesses)
- ❑ Familial history, parental age
- ❑ Work tasks or locations

15. OCCUPATIONAL HYGIENE RESOURCES

If on-going monitoring is conducted, the person(s) involved, currently or in the past, may have insights into the exposures for the subject being investigated.

- ❑ Name and contact information of person conducting monitoring

HOT TOPICS & EMERGING ISSUES
RISK AND HAZARD ASSESSMENT

Guideline on Occupational Exposure Reconstruction

Edited by Susan Marie Viet, Mark Stenzel, Christopher P. Rennix, Thomas W. Armstrong, and James R. Couch

The focus is on the industrial hygienist's role and integration with other contributors in exposure reconstruction projects. To maintain this focus the guideline presents current good practices in the development of efficient, yet thorough, procedures for any exposure reconstruction project. It addresses alternative approaches, data source considerations, exposure metrics, quality assurance, and appropriate documentation for possible future retrospective exposure data needs. Provided checklists will help ensure the collection of necessary information needed for later exposure assessment work and data analysis.

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