

Exposure estimation in four major epidemiologic studies in the acrylonitrile industry

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The reconstruction of worker exposures has been the mainstay of modern industrial epidemiologic studies. In most cases, the researchers are faced with the difficult dilemma created by the scarcity of the exposure measurement data vis-à-vis the demands for refined quantification. The 4 industrial epidemiologic studies of workers exposed to acrylonitrile share many similarities to illustrate strengths and weaknesses of the current exposure reconstruction methodologies. The analysis of the reported exposure reconstruction methods and comparative analysis of some of the results suggest that there is a certain degree of conformity in the results of the exposure reconstruction processes in these 4 studies. At the same time, the same analysis invokes some questions with respect to the interpretation of the exposure reconstruction results.

Key terms exposure levels, exposure reconstruction methods.

Starting from Sir Percival Pott, who linked scrotal cancer to chimney sweeping as an occupation (1), occupational health epidemiology has been a success story in discovering the causative factors in occupationally induced diseases. Between that seminal event and the coining of the phrase quantitative epidemiology by Professor Hatch in 1964 (2), many important developments rendered the simpler, more or less qualitative approach to occupational disease epidemiology less than desirable. It should be noted that this definition evolved in an era when considerably high exposures to potentially hazardous substances still existed in most workplaces. As workplaces became cleaner, the more-detailed questions about safe levels of low exposure to potentially harmful substances emerged. Consequently, the demands on obtaining quantitative exposure estimates in all epidemiologic studies became a constant feature. Obviously, with the availability of sufficient numbers of exposure and other determinant physicochemical measurements, it would be natural to expect the quantitative exposure measures to be a part of an epidemiologic study. However, epidemiologists may be, perhaps wrongly, criticized for the lack of a “thorough exposure assessment” even when the lack of data might not have permitted a realistic solution to the exposure reconstruction problem (3). In defining the problems proposed and analyzed in this paper, perhaps it is important to start with a direct quote from Professor Hatch (2): “How do we

identify environmental hazards, determine their magnitude and judge the adequacy of control measures? Certainly, *no physical measurements* can, in their own right, provide the answers; it is only because the factors *so measured* were first correlated with significant responses in man that they could, subsequently, be employed to identify and evaluate hazards and to assess the goodness of controls. . . . The demonstration of real relationships through systematic and, more particularly, quantitative epidemiological studies of exposed industrial populations, drawing upon skills in both the biological and physical areas, must be regarded, therefore, as one of the most significant contributions to occupational health” (Emphases added).

The lack of quantitative measurements and the remedies sought for this deficiency introduce some important problems with both practical and theoretical implications. Obviously, the only rigorous solution to the absence of data is to produce data by building simple or sophisticated substantive models of the processes, conditions, or tasks as they may have existed in the past. In this type of data production, any theoretical or mechanical models used must be based on physical or chemical principles. Clearly, the use of formulas with conjectured coefficients cannot be considered as data production; it is, simply, the quantification of conjectures in an organized manner. Ordinarily, model-based data production is a rarely used tool because of its complexity and cost.

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The more common methods of exposure reconstruction are based on the development of numbers to represent exposures based on available qualitative knowledge, quantitative but not directly related information about events in the past, analogy to other industries or industrial processes, and guess estimates in conjunction with sparse or unrelated or totally absent exposure measurement data. In the application of these methods, generally, the opinions of one or more knowledgeable persons are used to obtain numerical values for exposures. Operationally, the exposure reconstruction is achieved by a series of assigned values believed to be the exposure levels or presumed to be adjustments to some measurements. Thus these methods, for the most part, rely upon one or more sets of conjectures (4). All conjectural processes, from a psychometric point of view, are similar to the Delphi process of expert opinion formulation. The Delphi method was originally developed by Olaf Helmer and Norman Dalkey at the Rand Corporation to formalize the steps of achieving group consensus (5). The method was developed to induce a group to arrive at a relatively narrow set of opinions. However, the technique has been extended to many qualitative and quantitative forecastings using a group of task-oriented people (experts). In the application of the Delphi method to quantitative estimation or forecasting, there is a number of restrictions placed on the averaging procedures. Otherwise, interpretive difficulties arise from the differences in the comparative judgment of the experts. The nature of the quantification by Delphi or conjectural processes, the proper methods of scaling, and the proper averaging procedures have been well reported in the literature (6–9). The general availability of this information notwithstanding, to this author's knowledge, in the occupational hygiene applications of Delphi and other related conjectural processes, the mathematical details of scaling, averaging, and correlative methods have been ignored. Unfortunately, this seemingly arcane detail can result in extensive inconsistencies in group judgments and significant misinterpretation problems.

It may be useful to cite a few examples of conjectural methods commonly used in exposure reconstruction. The *traditional Delphi method* is a round-robin individual estimation by experts and reiterated modification of the forecasts to achieve a narrow range of opinions. In *group consensus* format forecast is made by inducing a group of experts to agree on a set of numbers through discussion. Often-used *professional judgment* uses one or more experts to provide independently formed opinions. *Group professional judgment* is essentially a nonstructured opinion poll of one to any number of experts on parts of a problem. Whether based on conjectured computational schemes, or labeled as professional judgment or under any other rubric, these and similar algorithms of exposure reconstruction share the properties of conjectural forecasting (10). The theorems used in the analysis and

comparison of conjectural processes and their interpretation are given in appendix I. Based on these theorems, 3 initial observations can be made: (i) in conjectural processes, the equivalence or nonequivalence of the results obtained does not connote correctness or exactitude; (ii) different conjectural approaches can create several sets of exposure levels for a given cohort such that the values cited in one set in complete disagreement with another set may not be determinably better or worse than the latter; (iii) the testing of only a portion of the potential range of reconstructed exposures is not necessarily a valid verification process.

If it is feasible, then it is desirable to find rigorous measures of believability for the conjecturally reconstructed exposures. Fundamentally, a carefully designed set of experiments can be used to challenge an appropriate set of predictions as a verification procedure for the extrapolated results. While this is the general principle of the scientific process (11), in exposure reconstruction studies, the experimental requirements that will rigorously measure the believability of a conjectural process may be unjustifiably expensive or extremely time-consuming and at times unrealistically complicated. In some cases, with known acute and observable effects of a compound, some measures of believability may be devised. For example, if a conjectured exposure level implies several fatalities would have occurred, then the lack of such a momentous event would cast doubt on the estimated values. As a verification procedure, often the comparison of conjectured results to some a priori measurements is used as a validation tool. Unfortunately, the comparison of the reconstructed exposures to extant data is not necessarily a valid verification of a conjectural process. Unless shown otherwise, it is likely that such a comparison would suffer from inadequate coverage problems and would be likely to create circumstances that suffer from the deficiencies of happenstance data correlation (12).

Clearly, labeling an exposure reconstruction method as a conjectural approach is not a pejorative statement. It is simply descriptive of its properties and states the need for rigorous analysis of the process and calls for the design of a valid verification method. In the absence or unreasonableness of a verification exercise, it would be necessary to attach a caveat upon the results stating that the values obtained are "best guess estimates within the knowledge available" and they do not necessarily connote a quantitative correctness.

Exposure reconstruction methodologies

At the onset it should be stated that the exposure estimation in all 4 major epidemiologic studies in the acrylonitrile industry represent different types of best effort with

scarce data resources. In that sense the criticism presented in this paper is more of a fundamental nature than specific in character. Any other approach in any one of these studies would have been a different, but not necessarily better or worse, approach.

The exposure reconstruction methods for the 4 epidemiologic studies and 1 limited corroborative study are referred to by the senior author's name in alphabetical order.

Benn

In Benn's study (13), exposure reconstruction was made by a simple grouping of job descriptions into 7 categories characterized by 3 acrylonitrile exposure levels. The determination of job categorization was based on plant personnel perception and the ranking of exposures. The exposure classes generated are strictly ordinal without a transformable scale. That is, one order cannot be transformed into another by an ordinary arithmetic operation.

Blair

In Blair's study (14), the investigators used a hierarchical procedure to establish the starting values for the exposure reconstruction process. For the starting values, the most preferred estimation is based on actual monitoring results, and the least preferred estimation is a guess estimate of a value by a knowledgeable person. Another but similar hierarchical procedure is used for the temporal reconstruction process, which can be characterized as variable, step size, multiplicative backward extrapolation. Any reconstructed value using an initial value is subjected to the same extrapolation. The extrapolating functions used are not necessarily derived from measurements or from physicochemical principles. The preferred hierarchy for extrapolating function generation is (i) monitoring, (ii) cross-plant comparison, (iii) exposure zone concept, (iv) significant change algorithm, (v) professional judgment. It is important to note that the numerical algorithms used to perform adjustments may be misinterpreted as empirical formulas derived with some technical basis. In this case, the formulas used are simply convenient expressions with the parameters that define the algorithms wholly conjectured (professional judgment). A validation procedure for the Blair method is described in the literature (15). However, this validation process is limited to the lower 10–15% (approximate) of the reconstructed range, and it does not seem to cover the domain (ie, all processes and tasks used in the reconstruction) adequately. Therefore, by theorem V (appendix I), the reported validation is not a proper one.

The final set of reconstructed exposures was scrutinized by several experts (internal and plant personnel) to keep the values that looked reasonable and to change the values that were perceived to be erroneous. This process is possibly the closest to the traditional Delphi process of

any one of the other processes used — albeit with complicated iterative steps to achieve consensus.

Esmen

The method used by Esmen (10) in exposure reconstruction is a perception test administered to selected plant personnel using an openly interpretable guide sheet (appendix II). The rating system and the explanatory phrases of the guide sheet were intentionally vague so as not to suggest an absolute scale. The purpose was to elicit information from the subjects with respect to how they perceived the exposures in very general terms. Because perception thresholds, acclimatization to odors, biological symptom thresholds, and remembrance of events in general are not particularly precise, to assign concentration scales to the perceived ranks would be fallacious. The measure obtained can only be translated into a transformable ordinal scale. No more than 14 employees who were very knowledgeable with the past processes and plant history were recruited by the plant or corporation contact for the facility. Approximately one-half of the test group consisted of "old timers" selected by the plant management or unions from the available pool of hourly workers and retired hourly workers. The other half was selected from the plant safety and health, engineering or administrative staff. After careful briefing of the group as to the purpose of the meeting, the test subjects were instructed in the particulars of the test they were about to take. It was explained and stressed that the "correctness" of the answers were not whether their responses agreed with the answers given by others or in comparison with a standard. After the explanations and the answering of any questions that arose, the group was individually given a list of 25 job classifications and an associated 3-year time span for each title. They rated each job-date combination without group discussion using the scale given in the guide sheet. The test takers would not have seen the job list or the classification prior to the first day's test. The testing during the second day was a repeat of the first day with 12 different jobs replacing a selected 12 from the first list. A different ordering of the jobs on the list was also provided. Only a few of the 13 repeat job titles had adjacent or overlapping but different dates than those of the first list; the remainder were identically copied from the first list. The results were analyzed for group consistency and tenacity by ordinary psychometric procedures.

Swaen

The exposure reconstruction by Swaen (3, 16) was based on the adjustment of existing exposure measurements with professional judgment of one or more industrial hygienists. The details of the reconstruction process were not available to this author. However, the brief descriptions of the exposure reconstruction process in the cited references suggest that data were extrapolated using a

substantial number of conjectural techniques. While the Blair and Swaen reconstruction processes may differ in detail, they seem to be equivalent in context. It is not clear that an iterative step as it was used in the Blair procedures was also used in this study.

Walrath

In Walrath's study (17), job classes were assigned data-based or conjectured exposure levels by an expert. These values were then reviewed by a panel of experts familiar with the operations. The lack of measurements for a very substantial portion of the study suggests that a great majority of the exposure assignments was through one or more conjectural processes. In this study, the reconstruction methods used can be viewed as group consensus with prompted input.

Data and information availability

One interesting observation pertains to the exposure characterization over time. In the 6 facilities examined by the author, among the subjects of the perception tests and the professional staff of the facilities interviewed, there was a

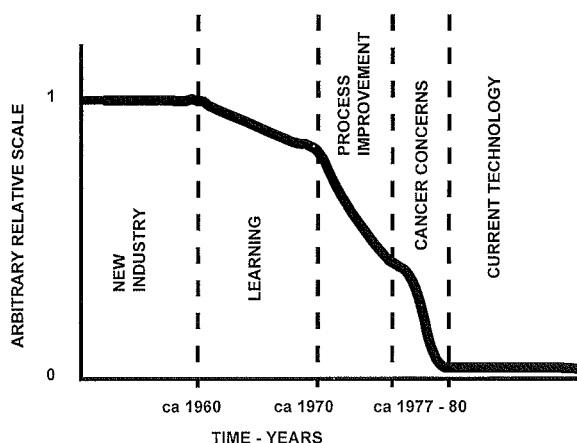


Figure 1. Graphic representation of the general trend of exposure to acrylonitrile.

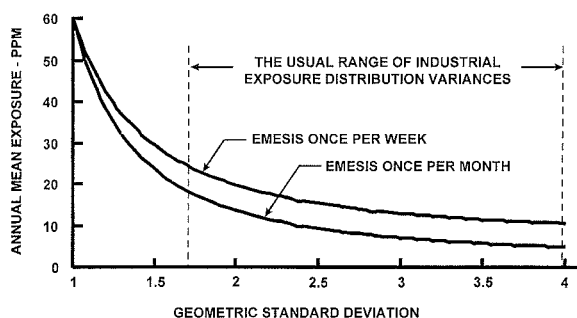


Figure 2. Calculation of the potential maximum value for individual annual mean exposure to acrylonitrile.

clear consensus that the general "high exposure experience" and "poor operating practices" were prevalent before about 1970, and there were some, perhaps significant operational improvements about 1970–1977 and very rapid improvement in the hygienic conditions between about 1978 and 1980. The improvements have been small but steady since then. These discussions suggest that, after the initial start-up and development problems of the industry until about 1960, there was a decade of learning to operate the system efficiently followed by process improvement. The health concerns publicized about 1977 apparently accelerated the improvements and the implementation of current technology (figure 1).

Acrylonitrile has an important biological acute effect that can be used to estimate the maximum potential for annual average exposure. Approximately 1-hour inhalation exposure to acrylonitrile at about 60 ppm is a strong emetic and is said to produce acrylonitrile "hangover" with severe headache. Noting that an annual average exposure is based on the mean of a distribution of exposures that can be used to estimate the integral that represents cumulative exposure (dose surrogate), the average value will, of necessity, have a variance associated with it. It has been shown that industrial exposures are realistically represented by a right-skewed distribution with a log-normal central limit (18, 19). With the assumption of a log-normal distribution, the annual mean exposures can be calculated as a function of the geometric standard deviation for one emesis expected per week and one emesis expected per month. The results of such a calculation are shown in figure 2. It is my opinion that one emesis per week would be intolerable for any one worker, and thus it would be reasonable to assume that the highest annual average exposure for any worker was probably considerably less than 20 ppm.

There seem to be very few actual exposure measurements that date back to the pre-1975–1978 era. While the lack of early personal exposure measurements in the Benn, Swaen, and Walrath studies are not specifically indicated in the references cited, there are sufficient implications which suggest that this was the case. In the Blair study, pre-1978 data for personal exposure is at best scant. Consequently, in the 18- to 21-year time span of the study, the more complete exposure data cover about the last 5 years when the exposures were reputed to be relatively low.

There is a reasonable number of measurements that seem to be available after about 1978. Even though there might be uneven emphasis on the sampling routines with respect to turn around, start up, and unusual exposure conditions, at least a representative selection of jobs seems to have been characterized through measurements. In the Blair study, possibly with the most measured exposures, approximately 15% of the estimates were based on measurements. Typically, the reconstruction of better than 80%

of the low exposures and virtually all very high exposures were produced by conjectural procedures.

Results of the Esmen and Blair study comparisons

Since I had full access to Blair data only, only a comparison between the Blair and Esmen methods has been carried out. The perception tests were carried out in 6 of the 8 facilities included in the Blair study. The perception test results and the corresponding year-specific Blair estimates were analyzed for individual plants, as well as in the aggregate. For the perception test, the interobserver consistency was determined by the relational coefficient of identity for absolute scales (20–21). The consistency between the judges, as measured by the relational coefficient, was 0.821 on the average, and this value did not vary appreciably from plant to plant (SD 0.049). The value of this coefficient ranges between -1.0 and 1.0, with 1.0 suggesting complete agreement and -1.0 suggesting complete disagreement among the judges. Therefore, the results suggest a remarkable consistency. The straight correlation coefficient for the group results from 1 day to the next was 0.948 on the average, and it did not vary more than 0.056, again indicating a remarkable consistency from 1 day to the next. The comparison between the Esmen and Blair results was performed by various methods. Of course, the simplest comparison is to compute the correlation coefficient between the 2 estimates. The correlation between the 2 sets of results was disappointing. The average correlation coefficient was 0.576 with a range of 0.478–0.656. Although the correlation coefficient is a general measure of trend, the rank preservation properties of the 2 methods would be more important. Of the 221 entries, 58.4% differed by 22 ranks or more. This qualitative test suggests that there is a potential for severe “misclassification”. By misclassification, it is simply implied that a qualitative exposure level suggested by one method is in disagreement with the qualitative level suggested by the other method. The level of disagreement can be investigated by another method of comparison. If one procedure is taken to be exact and misclassification that results from the other procedure is determined, then the rates and magnitudes of misclassification determined would imply the level of disagreement. It is important to stress the fact that none of these procedures *can claim the superiority of one procedure over another without properly designed verification*. Given this caveat, on the assumption that the reconstructed exposures by one of the procedures are exact, the 2 methods were compared. The results of this comparison are shown in table 1. Clearly, the finer the classification, the less agreement between the results of the 2 methods. The disagreement ranges between a low of 24% (high-low classification) to a high of 83% (6-category

classification). It must be noted that the disagreement between the results may be suggestive of a potential for misclassification. Since neither method has been properly verified, a relative agreement such as the one seen in the 2-way classification does not at all imply a lack of misclassification. One might be able to argue that the agreement between the results of 2 independent methods is comforting in the sense of a rational choice to believe the results.

Discussion and concluding remarks

Since the procedures used in the studies have a considerable resemblance, the results of the comparison between the Blair and Esmen methods can be assumed to apply to the rest of the studies. Clearly, the results shown in table 1 indicate that the procedures used are blunt instruments and open to criticism if the results are overinterpreted. In fact, the disagreement between the 2 methods is severe when the classification is extended over 6 classes, whereas a 3 or fewer category classification would be acceptably concordant. These measures apply to the exposed cohort only, and the unexposed cohort would probably be well determined by consensus. Depending upon the fraction of the estimates belonging to the unexposed categories, the overall agreement between the methods may be better than suggested. If the results are interpreted as a qualitative effort to reduce misclassification, then difficulties introduced by quantification would disappear. In that sense, if the results are not interpreted as “data” to be used in some mathematical formulation of risk assessment based on exposure response, then the exposure reconstruction efforts of each of these studies will take on their proper interpretation with respect to an exposure-response relationship.

Considering the rank ordering categorization only, one would expect good agreement between the Esmen and Benn methods; with the 4-category classification of the Swaen study, the disagreement between the Esmen and Swaen methods is probably higher than that of the Benn study. The disagreement between the Esmen and Walrath methods would be similar to that between the Esmen and

Table 1. Comparison of Esmen and Blair reconstruction for matched job-year pairs.

Number of classes	Cumulative misclassification potential by class difference (%)				
	1	2	3	4	5
2	24	-	-	-	-
3	38	2	-	-	-
4	71	38	6	-	-
5	83	53	8	0.5	-
6	83	48	18	3	0.5

Swaen study. It is important to note that, by the agreement or disagreement between the results, neither relative nor absolute accuracy is implied. Independently arrived consensus, while comforting, should not be mistaken for rigor.

The maximum exposure levels were reported in 3 studies. The maximum exposure level calculations agree with the maximum levels determined by the Blair and Swaen methods, but they disagree with the maximum annual average exposure reported by Walrath.

In view of the consistency of the judges within and between plants and a sensory basis for the conjectures, at least a significant number of readers may decide that the perception test is a more plausible conjectural method. This would be an incorrect conclusion. Nowhere in the construction of the perception test or in the results presented in this report is it suggested that the test is superior or inferior or equivalent to any of the other methods used. Such a conclusion would substantially misinterpret both the findings reported and my intentions.

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Appendix I

Theorems about conjectured processes

Definitions

Let C be a set of conjectured functionals in an exposure reconstruction process and T be the set of true functionals of the related exposure reconstruction process. The functions contained in T and C share the same domain, but they do not necessarily have the same range. The truth content of a conjectural process can be defined as $T \cap C$. Therefore, the amount of truth content of a conjectural process is the cardinal measure of its truth content $\mu(T \cap C)$. For any given exposure process x , let the exact set of exposures be $\{T(x)\}$ and let $\{\Theta(x)\}$ be the conjectured exposures translated onto $\{T(x), \varepsilon\}$ with a sufficiently small ε to preserve the order of $\{T(x)\}$. Note that, with this definition, biased estimates are allowed for but they require order preservation. This is a weaker condition than a requirement for exact estimation. However, it is a realistic requirement considering the utilization of $\{\Theta(x)\}$ in an epidemiologic study. Any conjectured set would be the union of two disjoint sets: $\{\Theta(x)\} = \{\Theta(x)\}^0 \cup \{\Theta(x)\}^1$ such that $\{\Theta(x)\}^0 \cap \{T(x)\} = \emptyset$ and $\{\Theta(x)\}^1 \subset \{T(x)\}$.

Consider the definition of a random assignment process such that if p is a randomly assigned value for r , then for any arbitrary r the probability $\Pr[p=r]$ is neither zero nor one, realistically. This statement implies that there exists a small $\varepsilon > 0$ such that $\varepsilon < \Pr[p=r] < 1 - \varepsilon$. By this definition, the exposure assignment process can be random in a strict sense, which requires an exact equivalence between p and r , or, in a heuristic sense, which requires p and r to be indistinguishable in the enumeration scheme used.

Theorem I

Random assignment of exposure implies $\mu(T \cap C) = 0$.

Proof. Suppose C is a random assignment process and $\mu(T \cap C) \neq 0$. Let $x \in T \cap C$, then $T(x) = \Theta(x) \Rightarrow \Pr[T(x) = \Theta(x)] = 1$ for all $x \in T \cap C$. This is a contradiction. QED.

Interpretation. If exposures are assigned at random, then there is no truth associated with the conjectural process.

Theorem II

$\mu(T \cap C) = 0$ is a necessary but not sufficient condition for $\{T(x)\} \cap \{\Theta(x)\} = \emptyset$.

Proof. By theorem I, the assignment process C is random only if $\mu(T \cap C) = 0$. However, it is not sufficient because, for any arbitrary x , $\Pr[T(x) = \Theta(x)] > \varepsilon$, by definition. QED.

Interpretation. Random assignment of exposure does not imply that some of the results obtained by random assignment would not be "correct".

Theorem III

For any 2 conjectural processes $C1$ and $C2$, $\{\Theta1(x)\} = \{\Theta2(x)\}$ does not necessarily imply that $\{T(x)\} \cap \{\Theta1(x)\} = \emptyset$.

Proof. Suppose $\mu(T \cap C1) = \mu(T \cap C2) = 0$. By definition $\Pr[\Theta1(x) = \Theta2(x)] > \varepsilon$ for some x . Therefore, by theorem II, $\{T(x)\} \cap \{\Theta1(x)\}$ is not necessarily empty. QED.

Interpretation. Between 2 conjectural processes the equivalence of the outcome does not connote correctness or exactitude.

Theorem IV

$\mu(T \cap C1) \neq \mu(T \cap C2)$ does not necessarily imply that $\{\Theta1(x)\} \neq \{\Theta2(x)\}$, and the converse is also true.

Proof. Suppose $C2 = C1 \cup Ca$ or $\mu(T \cap C1) \neq \mu(T \cap C2)$. But $\{\Theta2(x)\} = \{\Theta1(x)\}^0 \cup \{\Theta1(x)\}^1 \cup \{\Theta2(x)\}^0 \cup \{\Theta2(x)\}^1 - \{\Theta1(x)\}^1$. For any arbitrary $\theta a \in \{\Theta1(x)\}^0$ and any arbitrary $\theta b \in \{\Theta2(x)\}^0 \cup (\{\Theta2(x)\}^1 - \{\Theta1(x)\}^1)$ $\Pr[\theta a = \theta b] > \varepsilon$. Therefore in some cases $\mu(T \cap C1) \neq \mu(T \cap C2)$ and $\{\Theta1(x)\} = \{\Theta2(x)\}$ in some cases.

The proof of the converse is similar. Let, $\theta a \in \{\Theta1(x)\}^0$ and $\theta b \in \{\Theta2(x)\}^0$. Even with the strongest specification that $C1 = Ca \cup C$ and $C2 = Cb \cup C$ with Ca and Cb random processes, the $\Pr[\{\theta a\} = \{\theta b\}] < 1 - \varepsilon$. Therefore, $\mu(T \cap C1) = \mu(T \cap C2)$ and $\{\Theta1(x)\} \neq \{\Theta2(x)\}$ in some cases. QED.

Interpretation. There can be more than 1 conjectural process with different $\mu(T \cap Ci)$ that will give the same results, and, conversely, there can be more than 1 conjectural process with the same $\mu(T \cap Ci)$ that will give different results.

Corollary

Several conjectural processes can create several sets of results such that the values of 1 set would not be determinably better than any other. They would "just be different".

Theorem V

Let R be an absolute process such that $R \subset T$ and $C = C1 \cup C2$ with $C1 \cap C2 = \emptyset$ as a conjectural process.

$\{\Theta_1(x)\}=\{T_R(x)\}$ does not necessarily imply that $\{T(x)\} \cap \{\Theta_2(x)\} \neq \emptyset$.

Proof. Since C1 and C2 are independent, $\{\Theta_1(x)\}=\{T_R(x)\}$ does not specify that $\{\Theta_2(x)\} \neq \emptyset$.

Interpretation. If a portion of the values of a conjectural process that does not cover the domain of the conjectured values agrees perfectly with measured values, it does not necessarily imply that the untested portion will also agree. In a simpler manner, the testing of only a portion of the

potential range of reconstructed exposures is not a valid verification process.

Mathematical symbols used:

Implication - $\Rightarrow$

Subset - $\subset$

Element of - $\in$

Empty set - $\emptyset$

Union - $\cup$

Intersection - $\cap$

Appendix II

Perception guidelines used in the corroborative investigation

Exposure designation	Symptom or criterion description ^a
6	Smelled acrylonitrile 10 to 15 minutes at a time everyday — occasionally threw up during work — often had severe headaches
5	Smelled acrylonitrile 10 to 15 minutes at a time often — had acrylonitrile hangover once or twice a year — usually got acrylonitrile on workclothes
4	Smelled acrylonitrile 10 to 15 minutes at a time sometimes — at least more than once or twice per week smelled acrylonitrile but it was shorter in duration — sometimes got acrylonitrile on workclothes
3	Smelled acrylonitrile 10 to 15 minutes at a time occasionally — maybe once a week but definitely at least once a month got only a whiff of it — occasionally got acrylonitrile on workclothes
2	Smelled acrylonitrile rarely and less than 10 minutes at a time — maybe once a month or so got a whiff of it — once in a while got acrylonitrile on workclothes
1	Did not smell acrylonitrile at all — if very rarely smelled acrylonitrile, it was a whiff once in a while — generally worked in areas that had acrylonitrile but not all the time — very rarely if at all got acrylonitrile on workclothes
0	If exposed to acrylonitrile at all, it was only rarely and only for a very short time

^a"Exposed" means came into contact with acrylonitrile or breathed acrylonitrile vapor or was near machinery or equipment that used acrylonitrile or was near open acrylonitrile storage. "Occasionally" means once in a while. However, the occurrence must be repeated. Something happening only once in the times shown does not count as occasionally.