REPORT OF DAVID GARABRANT, M.D., M.P.H.

I, David Garabrant, M.D., M.P.H., state as follows:

1. I have been asked to review the relevant medical and scientific literature to determine whether or not there is reliable scientific evidence to support an opinion that there exists a cause and effect relationship between exposure to welding fume and the development of Parkinson’s Disease (PD) or parkinsonism. As set forth in more detail hereafter, it is my opinion that to a reasonable degree of scientific and epidemiological certainty, there is no reliable epidemiological evidence to support an opinion that exposure to welding fume is causally associated with the development of PD or parkinsonism. Therefore it is also my opinion that to a reasonable degree of scientific and epidemiological certainty, there is no reliable evidence to support an opinion that exposure to welding fume causes or accelerates the onset of PD or parkinsonism.

BACKGROUND, EDUCATION AND TRAINING

2. I am a professor of Occupational Medicine and Epidemiology at the University of Michigan School of Public Health. I have been on the faculty for 15 years and I have been a full professor since 1996. I am the director of the Occupational and Environmental
Epidemiology curriculum and the Center for Risk Science and Communication. At various times in the past 15 years I have also served as Director of the Occupational Medicine residency, the Industrial Health Program, and the Center for Occupational Health and Safety Engineering. Prior to my affiliation with the University of Michigan, I was a tenured faculty member at the University of Southern California School of Medicine.

3. I received my undergraduate education in chemical engineering at Tufts University and graduated in 1972. I then attended Tufts University School of Medicine and graduated in 1976. In 1979, I received a Master of Public Health degree from Harvard. In 1980, I received a Master of Science in Physiology also from Harvard University.

4. I completed a residency program in internal medicine at Georgetown from 1978 to 1980. I then was a resident in the specialty of occupational medicine at the Harvard School of Public Health from 1980 to 1981 before serving as a senior resident in internal medicine at the University Hospital in Boston. I am Board Certified in internal medicine, preventive medicine and occupational medicine.

5. In my current position at the University of Michigan, my time is divided into three areas. First, I see patients at the University of Michigan Medical Center. My practice is limited to occupational and environmental medicine, seeing patients who are ill and concerned about chemical or occupational exposures. Second, I teach graduate students at the School of Public Health and medical students. My third area of professional endeavor involves research. My research is in the area of environmental and occupational epidemiology. My research has been funded by the National Institutes of Health, the National Institute for Environmental Health Sciences, the National Institute for Occupational Safety and
Health, the State of California, United Auto Workers Ford Motor Company National Joint Committee, and the American Cancer Society, among others.

6. As an epidemiologist, I have researched and studied the relationship between pancreatic cancer and pesticides; environmental factors influencing breast cancer; mortality in the automobile manufacturing industry, lymphomas and transmission plant work; lung cancer and assembly plant work; lung cancer in welders; and neurologic effects of pesticides and solvents.

7. I have published over seventy 70 peer reviewed articles in scientific journals and over 150 scientific papers, abstracts, book chapters, and technical reports (see Curriculum Vitae and Bibliography attached as “Exhibit A”).

8. Attached as “Exhibit B” is a list of articles which I have reviewed on issues relating to manganese, welding, Parkinson’s Disease, and parkinsonism. I have also reviewed the reports filed in this proceeding by Drs. Levy, Louis, Wells, and Nausieda, and deposition and trial testimony by them and by Dr. Brad A. Racette in the Elam and Presler cases.

**PRINCIPLES OF EPIDEMIOLOGY**

9. Epidemiology is the branch of medical science that studies the patterns of disease in human populations and their relationship to various exposures. When relevant epidemiologic evidence exists, it must be considered before one can make a judgment about cause and effect between disease and an exposure. ‘Scientific Method’ is the established approach used by epidemiologists and other scientists to study the potential existence of a cause and effect relationship. It starts with an initial observation, sometimes from a case report (a person with disease and a particular exposure). From
there, a cause and effect hypothesis is developed. The hypothesis is then tested with properly conducted research studies with appropriate referent groups. These studies must rigorously test the hypothesis and seek to establish reproducibility.

10. There are many principles that must be observed to conduct a proper epidemiologic study. Generally speaking, these principles derive simply from the proposition that epidemiology is a science, and like all science, it depends on measurements, on precision, and on validity. An epidemiological study without proper measurements does not follow accepted scientific practice. An epidemiological study that cannot be independently verified by other researchers is not accepted by the scientific community because it cannot be determined whether it is reliable.

11. A proper epidemiological study must include clear definitions of both the disease (or more generally, the outcome) and the exposures that are under study. The outcome must be defined in a manner that is accepted within the medical community, typically based on physiological and pathological criteria. The diagnostic criteria must be reliably and consistently applied to all subjects included in the study. The exposure must be defined in such a way that determinations of which subjects have been exposed are both reliable and valid. The criteria for outcomes and exposures must be described by the researchers in sufficient detail that other qualified scientists can replicate their methods.

12. Epidemiologic studies have conceptual roots in scientific experimentation. When epidemiologic experiments are feasible, they are designed to reduce variation from extraneous factors (things not under study) compared to study factors. Most epidemiologic studies are non-experimental because of ethical and financial restrictions.
Nonetheless, the goal of non-experimental studies, like experimental studies, is to obtain valid evidence about the hypothesis under study.

13. There are two basic types of non-experimental epidemiologic studies. The cohort study is closely related conceptually to the experiment. Different exposure groups are compared to see whether their outcomes differ. The case control study compares people who have the outcome (or disease) to those who don’t have the outcome to see whether the groups differ in terms of their past exposures. In both types of study, there is a comparison or referent group. A principal goal of incorporating a referent group is to reduce variation from extraneous factors (things not under study) compared to study factors.

14. A cohort study typically begins by identifying a group who have been exposed to a particular substance (a potential cause of the disease) and a referent group who have not been exposed. The epidemiologist then compares the outcome (disease) rates in the exposed and non-exposed groups.

15. Case control studies are derived from a source population which hypothetically represents a source population in which a cohort study could be conducted. The cases are then identified and their previous exposure status is ascertained. The control group is selected as a representative sample of the source population that gave rise to the cases. The epidemiologist then compares the odds of exposure among the cases to the odds of exposure among the controls.

16. Cohort and case-control studies seek to determine whether there exists an association between an exposure and the disease being studied. An association exists when exposure and outcome (disease) occur together more frequently than would be expected by chance. For example, in a cohort study, there is an association when the disease rate in the exposed
group is higher than the disease rate in the non-exposed group. The disease rate in the non-exposed group represents the disease rate due to extraneous factors that are not under study and which are randomly distributed in the population (expected by chance). In a case-control study, an association exists when the frequency of exposure (or more correctly, the odds of exposure) is higher among the cases than it is among the controls. The existence of an association in an epidemiological study does not mean that there is cause and effect. Inferences about cause and effect require additional considerations.

Diseases have background rates in the general population, so that in any given group of people one would expect to find a certain number of cases of the disease in the absence of the exposure under study. Simply finding that some people who have a given exposure also have the disease does not prove any relationship between the two, and cannot serve as a basis for a scientist to conclude that the exposure is associated with the disease, much less causes the disease. Insofar as the disease has a background rate in the general population, the crucial question is whether people with a given exposure develop the disease more frequently than people without the exposure, and that can be determined only in properly conducted epidemiological studies.

In a case control study, the cardinal requirement of control selection is that controls must be sampled independently of their exposure status so that they represent the distribution of exposure in the source population from which the cases arose. The essential concept is that the exposure status of both cases and controls must be determined in a manner that is absolutely independent of their disease status.

An important corollary of the need for establishing disease status and exposure status independently of each other is that the diagnostic criteria for a disease cannot include the
exposure itself. For example, one might want to find out if swimming in an indoor pool caused respiratory infections. If one defined a disease as “swimming pool syndrome,” such that the diagnostic criteria were: (1) certain respiratory infections; and (2) having used an indoor swimming pool, then it would turn out that all persons who had this “disease” had used indoor swimming pools, and therefore the “disease” would occur more frequently among those who used indoor swimming pools than among the general population. But in fact one would have learned nothing; the observed “result” would be purely and simply the consequence of the improper disease definition, and the study would be uninformative. Valid epidemiological studies do not use disease definitions that include the exposure under investigation as a criterion for diagnosis.

20. A third central requirement of epidemiological studies is to avoid bias. Bias is the introduction of systematic error into the risk estimate as a result of improper study design. Selection bias occurs when cases are chosen in a manner that is not independent of their exposures or when controls are chosen in a manner such that they are not representative of the source population from which the cases arose. In either instance, selection bias can introduce a systematic error into the estimated association between outcome and exposure. Information bias occurs if the data is obtained in a different manner across study groups. For example, if the diagnostic evaluation, diagnostic criteria, or likelihood of seeking medical care differs between exposed and non-exposed subjects, the exposed group may have a higher chance of being classified as cases than the non-exposed group, simply because they different medical care. A second example would be if cases and controls were determined to have been exposed using different criteria or based on differences in the investigations of past exposures. If more (or different) effort was expended in
determining the past exposures of cases than of controls, this systematic difference would introduce error into the estimated association between outcome and exposure. Either type of bias will call the reliability of a study into question.

21. The existence or non-existence of an association is measured mathematically as a ‘relative risk.’ In a cohort study, that relative risk can be expressed numerically as a standardized incidence ratio (“SIR”), a standardized mortality ratio (“SMR”), a proportionate mortality ratio (“PMR”), or a standardized hospitalization ratio (“SHR”). Each is calculated by dividing the number of incident cases of disease (or deaths) by the number of incident cases of disease (or deaths) that would be expected if the study population had the same disease rate (or mortality rate) as the referent population. If, for example, 6 of 100 individuals in an exposed population develop disease each year and 15 of 500 individuals in the referent population develop the same disease each year, the SIR would be calculated as follows:

\[
\text{Observed cases (OBS)} = 6 \\
\text{Expected cases (EXP)} = \text{incidence rate in referent group (15/500)} \times \text{(100 persons)} \times \text{(1 year)} = 3 \\
\text{SIR} = 6/3 = 2.0
\]

An SIR above 1.0 suggests the existence of an association between the exposure and the disease in question. An SIR of 1.0 indicates that no association exists and an SIR of less than 1.0 suggests that the agent is associated with reduced risk of disease.

22. In a case control study, the potential existence of an association is measured by the

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1 ‘Relative risk’ is an umbrella term used to describe the various measurements of association utilized in both cohort and case-control studies, including SMR, SIR, PMR, OR, etc.
calculation of an odds ratio (“OR”). An odds ratio is determined by a comparison of the odds that a case (person with a disease) was exposed, to the odds that a control (person without disease) was exposed. If, for example, among 10 cases 5 were exposed and 5 were not exposed, the odds of exposure among cases would be $5/5=1.0$. If, among 12 controls, 3 were exposed and 9 were not exposed, the odds of exposure among controls would be $3/9 = 0.33$. The odds ratio is the ratio of the odds among cases to the odds among controls.

$$OR = 1.0/0.33 = 3.0$$

An OR above 1.0 suggests the existence of an association between the exposure and the disease in question. An OR of 1.0 indicates that no association exists and an OR of less than 1.0 suggests that the agent is associated with reduced risk of disease.

**TESTING THE RELIABILITY OF AN ASSOCIATION**

23. If an epidemiological study finds the existence of an association, the reliability of this conclusion must be tested by evaluating the possibility of bias, confounding and chance as explanations for the association.

24. Bias indicates the existence of a systematic error that may affect the reliability of the results. The following scenario is illustrative of an ‘information bias,’ i.e., a bias created by a disparate quality or intensity of measurements between the observed and referent populations:

A researcher is investigating an association between work in petroleum refineries and prostate cancer. In doing so, she asks each male refinery employee to undergo a physical examination, transurethral ultrasound, CT and blood screen for PSA. The researcher then compares the prevalence of prostate cancer in the refinery population with the prevalence in the referent or general population (most of whom have not been subjected to such a thorough diagnostic evaluation). The
intensive screening in one population and the lack of comparable observations in
the referent population results in an apparently higher prevalence of prostate
cancer in the refinery population than in the referent population.

25. Selection bias refers to any distortion of an exposure-response association that results
from the procedures used to select subjects, or that results from the factors that influence
study participation. The following scenario is illustrative of a ‘selection bias,’ i.e., a bias
created by disparate criteria for sampling from the exposed and referent populations.

A researcher is investigating an association between work in petroleum refineries
and prostate cancer. The refinery employees who comprise the exposed
population are identified based upon a screening questionnaire that asks whether
they have any urinary symptoms. The referent population consists of individuals
who have been randomly selected from the local telephone directory. The
researcher then compares the prevalence of prostate cancer in both groups. In the
refinery population, the use of a screening questionnaire has led to the selection of
subjects who are more likely to have prostate cancer (because it causes urinary
symptoms). In the referent population, there is no such selection. This selection
bias leads to an apparent association between work in the refinery and prostate
cancer. It also violates the requirement that exposure status and disease status be
established independently of each other.

26. Confounding occurs when there is some factor, other than what is being studied, that
distorts the apparent association between an exposure and a disease. For example, if a
study finds that work on the night shift is associated with colon cancer, and the study did
not consider the difference in exercise habits of people who work night shifts, it might
appear as if working the night shift was associated with colon cancer when, in fact, the
association is due to exercise habits. In this instance, if people who work the day shift get
more exercise than those who work the night shift, and lack of exercise puts people at
increased risk of colon cancer, then exercise confounds (or distorts) the relationship
between work on the night shift and colon cancer.

27. It is essential to evaluate the role of chance as a possible explanation for an association.
To assess whether or not an association (elevated SIR or OR above 1.0) is reasonably
consistent with chance, epidemiologists determine the statistical significance of the study results by calculating a ‘p-value’. The p-value measures the probability that the data (from which the association is estimated) could occur by chance when there is, in fact, no association. Epidemiologists typically require a p-value of .05 or less to conclude that the results are unlikely to be due to chance.

Epidemiologists also calculate a ‘confidence interval’ to assess the role of chance as well as to provide a range within which the true OR is believed to be likely to fall. For example, if an epidemiologist observes an OR of 1.5 and the 95% confidence interval is 1.0 to 2.25, it means that the epidemiologist is 95% confident that the true odds ratio falls between 1.0 and 2.25. If the lower confidence limit is below 1.0, then the investigator concludes that there is a reasonable likelihood that the true odds ratio may also be 1.0 (i.e., no association). In other words, the investigator properly concludes that the data obtained are reasonably consistent with there being no true association.

If the investigator looks for and fails to find evidence of bias and confounding and finds the results are reasonably inconsistent with chance as an explanation, it still does not establish a causal relationship between an exposure and a disease. It simply means that there is neither an obvious systematic error nor a random error that explains the observed association. An epidemiologist, in assessing causation, would then consider other factors such as temporal relationship; strength of the association; dose-response relationship; replication of the findings; biological plausibility; consideration of alternative explanation; cessation of exposure; specificity of the association; and consistency with other knowledge. These factors are known as the ‘Bradford Hill’ factors, after the English epidemiologist who published an influential article defining them. The Bradford Hill
factors are used because not all observed associations are causally related, so that the fact that an association exists does not by itself establish that causation is present. Accordingly, they come into play only when an association has first been established by epidemiological evidence.

30. Case reports typically describe a single individual or a series of individuals who have coincident exposure and disease and who are regarded by the observer as unusual in some way. Such reports do not provide evidence of associations in which the role of chance, bias or confounding can be evaluated. As a result, case reports are not regarded by the scientific community as providing evidence of causation, nor are they regarded as reliable scientific evidence. Case reports often play a valuable role in the scientific community insofar as they generate hypotheses that can be tested by rigorous, well designed scientific studies.

**PARKINSON’S DISEASE AND PARKINSONISM AMONG WELDERS**

31. Welding is a fairly common occupation. The U.S. Department of Labor, Bureau of Labor Statistics indicates there were about 452,000 welding, soldering, and brazing workers in 2002. Millions of other people have done some welding.

32. A number of studies have attempted to determine the background rates of Parkinson’s Disease (“PD”) and parkinsonism. These studies present data from different countries around the world. They suggest that the incidence and prevalence of these diseases may vary depending on factors not fully understood. Incidence and prevalence certainly vary depending on age, race, and sex. The studies agree, however, that PD and parkinsonism are not rare. The most recent study, in the Netherlands, suggests that 8.5% of all men over
55 will develop some parkinsonism, of whom slightly more than half will develop PD. De Lau (2004). Accordingly, in the large population of men who have done some welding, one might expect to find thousands of cases of PD or parkinsonism, even if the prevalence of PD and parkinsonism among welders is no different than it is in the general population. The mere fact that some welders suffer from PD or parkinsonism, accordingly, does not establish any causal relationship between welding and PD or parkinsonism; it could easily be the result of chance. Accordingly, in order to determine, to a reasonable degree of medical or scientific certainty, whether there is an association between welding and PD or parkinsonism, it is necessary to do proper epidemiological studies. In the next section I discuss the studies that have been done.

**RELEVANT EPIDEMIOLOGIC STUDIES**

33. I have reviewed 14 epidemiological studies that found no reliable association between welding and Parkinson’s Disease or parkinsonism.

   a. [Redacted]

   This section temporarily redacted in order to in order to comply with a court-imposed confidentiality order.
b. The Park/Kim Studies

Drs. Park and Kim, et al. published two articles in 2004 reporting the results of a large hospital-based case-control study in South Korea. Three hundred sixty-seven PD patients and 309 controls were interviewed about occupational history, lifestyle, family history, and education level. The study found that occupations with a high potential exposure to Mn, including welding, showed consistently negative association with PD after adjusting the confounders such as age, sex, smoking, and education level. (OR: 0.42, 95% CI 0.22-0.81).

c. The Tsui Study

A 1999 case-control study by Dr. Joseph Tsui evaluated whether occupations, including welding, were associated with an increased risk of PD among the general population of Vancouver, British Columbia, Canada. The occupations of 441 PD cases and 6,659 controls (who did not have PD) were ascertained. Although Dr. Tsui reported associations between PD and numerous occupations, welding was not among those found to be associated with PD. This very large study does not support a conclusion that welders are at increased risk of PD.

d. The Tanner Study

A 2003 case-control study by Dr. Carolyn Tanner evaluated whether several occupations, including welding, were associated with an increased risk of PD. Dr. Tanner studied World War II veteran twin pairs where one twin had PD and the
other twin did not. The study is particularly relevant because more welding took place during World War II than during any other time in the nation’s history. Dr. Tanner’s study indicated that welding was not associated with an increased risk of PD.

e. The Goldman / Olanow Study

Drs. Goldman and Olanow, et al. published a study in 2004 that surveyed the medical records of 1087 consecutive PD patients seen between 2000 and 2002 at the Parkinson’s Institute in Sunnyvale, CA. The study looked to determine if welding was associated with an earlier age of PD onset. Of 885 records containing both primary occupation and age at onset information, the most common occupation was teaching (11.8%), followed by administrative workers (10.5%), engineers (9.9%), sales workers (9.1%), and managers (8.7%). In contrast, only 0.2% were welders, 0.5% machinists, and 3% construction workers. The risk of PD onset at less than age 50 was significantly increased only for technical workers. The authors concluded that welding was not associated with an earlier onset of PD in the clinical population they studied.

f. The Dreessen Study

In 1947, Dr. Waldemar C. Dreessen presented the results of an investigation by the U.S. Maritime Commission into the health hazards of shipyard arc welders who engaged in mild steel and galvanized steel welding. A total of 4,650 individuals from seven different shipyards received physical examinations. One fourth of this group was comprised of non-welders who served as the control group. A total of 246 workers had done some welding before coming to work at the shipyard. Fume
concentrations in the air were measured, and the report stated that mild steel welding fume contains, among other compounds, 2-12% manganese oxide. No neurological problems were noted among this group of welders who engaged in a significant amount of welding.

g. The Walrath Study

In a 1985 cohort study, Dr. Judy Walrath examined mortality patterns among U.S. Veterans classified by occupation. Despite the high level of welding that took place during World War II, PD was not the cause of death in any of the 771 veterans classified as a welder or flame cutter.

h. The Coggon Study

In 1995, Coggon, et al., reported on causes of death among welders in Great Britain between 1979 and 1990. The data were part of the most recent reporting on occupational mortality by the British government over the past 150 years. Welders were at no clearly increased risk of diseases of the nervous system and sense organs (PMR = 1.04, 95% CI 0.84-1.28).

i. The Milham Study

In 1997, Milham reported on mortality in Washington State, in which he analyzed the death certificates of 588,090 men and 88,071 women who died between 1950 and 1989. Milham found only four cases of PD among welders and flame cutters — with roughly eight expected. The proportional mortality ratio (PMR) was 0.49 and the 95% confidence interval was 0.13-1.26, consistent with no association between Parkinson’s disease and welding.

j. The Kirkey Study
In 2001, Kirkey reported on a case-control study of PD derived from a source population of 239,722 individuals enrolled in a health care system in Michigan. PD cases and controls were interviewed about their lifetime occupational histories. Kirkey reported no findings showing an association between welding and PD.

k. The Kizer Study

In 1987, Kizer reported the results of a mortality study covering the population of California. A detailed investigation of the pattern of mortality was reported for welders, cutters, solderers, and brazers. Among 1,086 male deaths in this occupational category, there was no evidence of increased risk of PD or parkinsonism reported.

l. The Fall Study

In 1999, Fall reported a case control study of 113 PD cases and 263 controls that were derived from a source population of 147,777 in southeastern Sweden. The subjects answered questions about their occupational history and time spent in different jobs. The jobs and occupational exposures under study specifically included metal workers. A significantly reduced risk was found for metal workers (OR = 0.34, 95% confidence interval 0.12-0.82).

m. The Hertzman Study

In 1994, Hertzman reported a case control study of 127 PD cases and 245 controls derived from the population of British Columbia, Canada. Interviewers administered a questionnaire regarding occupational and chemical exposures to all subjects. The authors reported no significant associations between PD and exposure to heavy metals. Contact with manganese was reported specifically and
was not found to be associated with PD (OR = 0.83, 95% confidence interval 0.49-1.40 among men and OR = 0.92, 95% confidence interval 0.65-1.31 among women).

n. The Schulte Study

In 1996, Schulte and colleagues at the U.S. National Institute for Occupational Safety and Health (NIOSH) reported results from the National Occupational Mortality System which included deaths from 27 states between 1982 and 1991. The study included 43,425 deaths due to PD. The ten highest ranked occupations for risk of PD were reported and welders were not among them.

34. I am aware of certain case reports that have reported that manganese miners and other workers exposed to very large doses of manganese have developed a rare form of parkinsonism sometimes called “manganism”. No reliable epidemiological study of which I am aware has found any association between welding and manganism. This section temporarily redacted in order to in order to comply with a court-imposed confidentiality order.

I do not regard it as medically impossible that a welder, exposed to fume containing a high manganese content, and working in a confined space with inadequate ventilation, might inhale enough manganese in a short period of time to produce manganism. That does not change the fact that there is an entire absence of reliable epidemiological studies that show that manganism (or any other form of parkinsonism, for that matter) is associated with welding, and that no such association may be assumed in the absence of such studies.
PLAINTIFFS’ MATERIALS

35. I have reviewed a published article and two abstracts by Dr. Racette, and also the expert reports of Drs. Levy and Louis previously filed in this proceeding. None of these materials alter my opinion that there is no reliable scientific or epidemiological evidence that there is an association, let alone a causal association, between welding and PD or parkinsonism. On the contrary, these materials do not follow generally accepted scientific or epidemiological methodology, have evident errors or biases, and do not provide reliable bases for their conclusions.

36. Racette (2001) puts forward the hypothesis that exposure to welding may accelerate the onset of PD. As Racette himself acknowledges, his study does not prove the existence of the relationship he hypothesizes, and “a detailed clinical evaluation of career welders compared with age-matched controls in a proper epidemiologic study will be essential to prove the relationship between welding and parkinsonism.” On page 12 of his paper, Racette stated his hypothesis that welding may accelerate the onset of PD, based on a comparison of 15 career welders with parkinsonism from the Movement Disorders Center at Washington University in St. Louis with “control” groups of other patients from the same Center diagnosed with idiopathic PD. This comparison is not reliable because of selection bias. In order to estimate the age distribution of parkinsonism among welders, a researcher would properly conduct a study in which a cohort of welders is followed over time and the age-specific incidence rates of parkinsonism in the entire cohort are then calculated. Identical follow-up and calculations would be made in a reference population of non-welders and the age-specific incidence rates would then be compared between welders and non-welders. This would give a valid estimate of whether welders had
younger age at onset of parkinsonism. This is not what Racette did. Instead, he relied on a convenience sample of welders from his Movement Disorders Center. There is no reason to believe that this group was representative of the experience of welders with respect to parkinsonism. In fact there are reasons to believe that bias is likely in his convenience sample. It should be noted that welders must be able to:

- Hold their hands and arms steady while welding, or hold their hand steady while moving the arm
- Use hands and fingers to grasp and assemble objects
- Make quick, precise adjustments to machine controls
- React quickly and make fast, repeated movements of fingers and hands
- Keep or regain body balance or stay upright when in unstable positions

Tremor, rigidity, slowness of movement, and postural instability (cardinal signs of parkinsonism) would quickly interfere with the livelihood of a welder. Other careers that do not require such manual skills, coordination, and balance would not be similarly jeopardized. Thus, a welder with parkinsonism would seek medical attention early in his disease, while other workers might not. This difference in propensity to seek medical care would result in observation bias, making welders appear to have a younger age at onset of parkinsonism.

Selection bias also arises in the study design used by Racette. When an investigator compares two different groups in terms of disease characteristics, the comparison is valid only when the two groups have the same age distribution (unless the investigator controls for differences in age between the groups by making age-specific comparisons, or unless the disease does not vary by age). If the two groups have different age distributions, the
two groups may differ in their disease characteristics simply because of age differences. Racette studied 15 welders with parkinsonism, requiring that subjects satisfy two criteria to be included: they must have been career welders and they must have had parkinsonism. His comparison group was required only to have parkinsonism. Because welders, on average, are younger than patients with parkinsonism, this difference in selection criteria may create a difference in age between the two groups. Thus, the difference in age between welders with parkinsonism and other patients with parkinsonism in the Racette study is not a reliable scientific observation because of the likelihood that it is simply due to selection bias. Two other studies that properly controlled for age have found no association between welding and early onset of PD. Blot (2004); Goldman/Olanow (2004).

38. When Racette compared welders with other parkinsonism patients (whether matched on age or not) there were no differences in the severity of disease or the frequency of the cardinal features of Parkinson’s Disease. These findings indicate that the clinical presentation of parkinsonism was not meaningfully different among the groups studied.

39. Racette (2004A) is an abstract, and does not provide sufficient information to evaluate the validity of the study Racette describes. If and when Racette publishes the study described in this abstract, I expect to comment further on Racette’s method and conclusions.

40. The reports of Drs. Levy and Louis also do not provide any reliable epidemiological evidence for the proposition that there is an association between exposure to welding fume and PD or parkinsonism.

41. Dr. Levy’s report neither presents nor discusses any epidemiological evidence concerning the relationship between exposure to welding fume and parkinsonism or PD. In his report
he relies on a single article from the medical literature that deals with welders, Beintker (1933), which is a case report, not a properly conducted epidemiological study. Instead, he bases his conclusions on his belief that there is a “mechanism of injury,” which he describes. Whatever the merits of this belief, he has failed to consider the relevant epidemiological studies that would inform his opinion. Opinions that fail to consider relevant and reliable scientific evidence do not meet accepted standards of conduct among scientists. Many biologically plausible mechanisms of injury exist which do not in fact cause disease, or do not cause a particular disease. Even if a biologically plausible mechanism of injury exists, one cannot conclude that an association exists in fact between a particular exposure and a disease without properly conducted epidemiological studies that show associations that are not reasonably explained by bias, confounding, or chance. Levy neither presents nor discusses any such study.

42. Dr. Louis at least mentions epidemiological studies, but relies on only three. Racette (2004); Gorell (1997); Seidler (1996). None provides reliable evidence of any association between welding and PD or parkinsonism. I have previously discussed Racette (2004). Gorell (1997) found associations between ten variables and PD, one of which was exposure to manganese for more than 20 years. When Gorell (2004) re-analyzed the data, he found that there was no clear association between manganese exposure and PD. This demonstrated that once appropriate analyses were done (which controlled for correlated exposures), the apparent association between PD and exposure to manganese in the first Gorell (1997) study was spurious. Seidler (1996) recruited PD patients in nine nursing homes and compared patients and controls with respect to exposure to a number of substances; the focus of the study was on pesticides and wood preservatives, but questions
were asked about heavy metals, including manganese. When the investigators asked for the subjective recollection of the subjects, 5 patients and one control reported some exposure to manganese. However, Seidler and his coworkers also evaluated exposures using a Job Exposure Matrix based on expert assessments of exposure. Using this measure of exposure, they found no association between PD and exposure to any heavy metal.

CONCLUSION

43. Welding has been studied extensively throughout its history. A review of the medical and scientific literature does not reveal any reliable association between welding and PD or parkinsonism. Insofar as there is no reliable evidence that welding and PD or parkinsonism are associated, there is no evidence that they are causally associated. Based on the foregoing, it is my opinion to a reasonable degree of scientific and epidemiological certainty that there is no reliable evidence to support an opinion that welding fumes cause or accelerate the onset of PD or parkinsonism.

RULE 26 DISCLOSURES

44. My hourly rate for consulting in this matter is $525, with the exception of depositions and court testimony, for which my rate is $2,250 per half day (up to 3.5 hours of testimony).

45. A list of my prior testimony since January 2000 is attached as Exhibit C.

DATE  

DAVID GARABRANT, M.D., M.P.H.