

Cancer Risk among Wafer Fabrication Workers In the Semiconductor Industry

**Evaluation of Existing Data
And Recommended Future Research**

Executive Summary

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Executive Summary

Charge:

The Scientific Advisory Committee (SAC) was charged to evaluate possible cancer risk among wafer fabrication workers in the semiconductor industry from a review of available scientific information. If current information was judged to be inadequate, then the SAC was charged to determine what further study, if any, might be useful to evaluate cancer risks associated with occupational exposures to chemical agents or ionizing radiation in wafer fabrication.

Findings

In the one published study that has examined cancer risk among semiconductor workers, wafer fabrication workers were not specifically identified. No clear excesses of site-specific cancer risk were found although the study was small and had limited follow-up. There are two ongoing studies, a small one sponsored by the Health and Safety Executive in the UK and a larger one by IBM in the US, neither of which had preliminary results available for this review.

In the absence of studies that directly address risk of cancer in wafer fabrication settings, the SAC undertook a review of processes and chemical use in these settings. From among more than 200 agents identified, we focused our attention on 26 determined to be definite, probable or possible carcinogens by the International Agency for Research on Cancer. For these agents, we reviewed all relevant *in vitro*, animal, and epidemiologic data available in the published literature. To help characterize cancer risk among wafer fabrication workers, the literature was supplemented by material provided by SIA describing the process history of semiconductor device manufacturing as well as data on estimated amounts used and ranges of possible exposures. Some general patterns of exposure were clear; the highest values were most often found in maintenance tasks, whereas measurements made during normal operations in wafer fabrication were commonly below the range of data in the published literature. There was considerable uncertainty, however, about specific agents present in early wafer fabrication (as far back as 30-40 years ago), about exposure levels during that early time period and about agents generated as by-products throughout the history of the industry.

Conclusions

1. There is no affirmative evidence at the present time to support the contention that workplace exposures to chemicals or other hazards in wafer fabrication, now or historically, measurably increase the risk for cancer in general, or for any particular form or type of cancer.
2. Conversely, there is insufficient evidence at the present time to conclude that exposures to chemicals and other hazards in wafer fabrication have not or could not result in measurably increased risk of one or more cancer types.

There are two fundamental limitations to existing knowledge that have led the SAC to this second conclusion: a) Available exposure information did not preclude the possibility that some subgroups of workers may have had undocumented exposures to agents of concern at higher levels with non-negligible potential for cancer risk (e.g., as unknown reaction byproducts or from episodic spills); b) In view of the number of agents, agent combinations and possible chemical by-products created during wafer fabrication, the SAC concludes that a standard agent by agent risk assessment would not adequately answer questions of cancer risks in wafer fabrication. The inadequacies are a result of the enormous uncertainties of extrapolation from relatively high doses (seen in other settings) to much lower doses, as well as the absence of valid risk assessment models suitable for addressing carcinogenic potential of mixed exposures that may act synergistically. Because mixed exposure effects are an important feature of the exposure environments in wafer fabrication, a standard risk assessment could very plausibly lead to inaccurate estimates of predicted overall risk.

Recommendations

The SAC has determined 1) that a rigorous epidemiologic study is desirable to evaluate the cancer risk to workers in the wafer fabrication areas and 2) that development and support of ongoing health surveillance activities be undertaken at all company locations.

Study of Cancer Risk: The SAC recommends that the SIA commission an epidemiologic cohort study of wafer fabrication workers to answer the following three questions: a) Have wafer fabrication workers, as a group, experienced excessive risks of specific types of cancer? b) Has there been excess cancer risk among particular segments of the wafer fabrication workforce, defined by process type or job? c) Are there exposure-response relations for specific cancers where increasing risk is associated with increasing length of employment in wafer fabrication, or in particular processes or jobs, or with increasing level of exposure to specific agents?

An historical cohort mortality study, with integrated nested case-control studies is recommended as the most appropriate approach. Such a study is likely to generate the most useful information in a reasonable period of time. Although the primary focus of study is cancer, the cohort mortality study should also include an evaluation of risks for non-cancer outcomes. This would provide the most complete examination of mortality in wafer fabrication workers. The SAC's preliminary estimates of cohort size indicate that a cohort study would likely have sufficient statistical power to detect elevated cancer risks and dose-response trends for the more common cancers. In addition, from the SAC's review of personnel, work history, and industrial hygiene monitoring data provided by six SIA member companies, it appears that the employment and minimal exposure records needed to conduct a retrospective cohort study are likely to be available.

Because mortality studies are less than ideal for studying cancers with good survival, e.g., breast and prostate cancers, SAC also recommends a cancer incidence study using a subset of the same cohort located in regions with population-based cancer registries. Both the mortality and cancer incidence studies should also be updated by further follow-up five to ten years later. Particularly for the less common cancers, additional years of observation and latency may be needed to address the complete range of questions about cancer risk. In

addition, prospective surveillance of cancer mortality and incidence among employees hired after the study cohort is defined will be highly beneficial for examining cancer risks as they may relate to contemporary exposures.

The proposed epidemiologic study should be based on a defined cohort of wafer fabrication workers that includes as many workers as can be identified from the earliest date of wafer fabrication production in participating companies. To this end, it is recommended that member companies suspend any planned or periodic destruction of employment, work history, exposure assessment, or medical records.

Development of a plant- or location-specific job-exposure matrix that can be linked with work history data will be essential to reconstruct agent-specific exposures that ultimately will be investigated in subcohort or nested case-control analyses of selected cancers. In general, cancers to include in nested studies would be chosen based on preliminary findings of possible excesses of specific types of cancer in the cohort study. As there are no a priori hypotheses at this stage, thus decisions about which cancers to study with the nested case-control design should be deferred until findings emerge from the cohort analyses. An exception might be a cancer, such as lung cancer, which might be of interest because of its relatively high frequency and its association with higher levels of exposure to agents used in the semiconductor industry (e.g., arsenic).

Should the SIA accept this recommendation, a Request for Proposals (RFP) should be issued for open bidding by qualified investigators. The SAC suggests that the RFP include plans for a two-phased epidemiologic cohort study of wafer fabrication workers: a scoping phase and, depending on determination of feasibility, a full epidemiologic study. Plans for further studies, will depend upon the conclusions of the historical cohort study.

Ongoing Health Surveillance - Data Collection Infrastructure The SAC endorses development and support of ongoing health surveillance activities as early warning systems for occupational disease. To facilitate the process, the SAC recommends SIA designate a working group to benchmark large corporations known to leaders in medical surveillance schemes to investigate approaches currently in use, and provide findings to member organization.

With the advent of health care management systems (generally introduced to assist human resources (HR) departments in provision of managed health care benefits), new and potentially more powerful tools have been developed. When linked to personnel files -- assuming these provide information about current and past jobs in sufficient detail to translate into some measure of exposure through linkage to available exposure information -- the health records offer a potentially invaluable resource for monitoring a wide range of diseases and injuries.

The availability of electronic linkage to meaningful exposure groupings allows ongoing comparison of the incidence and prevalence of these conditions in the workforce of interest and comparison of rates in one location or job type to another. Such systems are only as good as the quality of the data entered and meticulousness of data management. Moreover, thoughtful querying of databases will always be required to produce meaningful information

about exposure-related health risks. Nonetheless, the cost of implementing and maintaining such systems, which is often highly beneficial to HR and other corporate entities, is quite low, and the utility to note problems and to launch early investigations is correspondingly high.

Proposed Next Steps

Scoping Phase: Because the scope of the SAC's review of employment and other records was limited for logistical reasons, there remains some uncertainty as to the size and characteristics of a potential cohort of semiconductor manufacturing workers to study. For this reason, the SAC recommends a two-stage process starting with a scoping study that would provide more detailed information about availability of existing records needed for different study approaches and the feasibility of each study type.

In the scoping phase, the contractors would validate the feasibility and propose a study design after on-site review of personnel and work history records at locations of confirmed participants. This effort would a) verify the cohort size and completeness of the cohort, b) determine the work history record availability, form, and time-period covered for members of the cohort, and c) evaluate available industrial hygiene exposure data at participating companies. If a further, full-scale epidemiologic study is recommended, the scoping phase investigators would prepare a detailed research protocol with an accompanying budget request and justification. The protocol would be reviewed for scientific merit.

Selecting a Contractor: Selection of a qualified contractor to carry out the scoping phase and the epidemiologic study, if determined feasible, would probably require appointment of a Scientific Advisory Committee to prepare a Request for Proposals. This committee would identify the manner in which the RFP is advertised, review submitted proposals, recommend contractors, finalize the study scope of work, oversee the technical aspects of the study, and serve as liaison to the SIA during the execution of the study.

Facilitating the Study of Cancer Risk: To facilitate this recommendation, we recommend identifying a small number of current employees with the appropriate experience to gather personnel, job history, and exposure records, identify and catalog information on the history of employment, job assignments and responsibilities, and work processes. In some instances, records ownership could take some time to resolve, and should probably be addressed by the SIA before an investigator gets involved. Each company is encouraged to develop an oral history of its operations because such information will prove valuable for the proposed research.