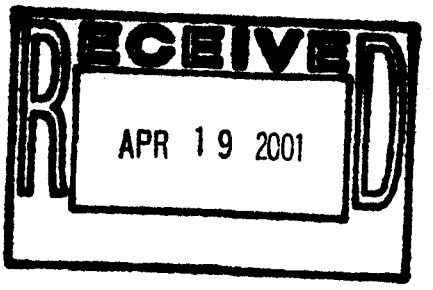
UAB SCHOOL OF PUBLIC HEALTH

Department of Epidemiology

April 18, 2001



Dr. C. W. Jameson
National Toxicology Program Report on Carcinogens
MD-EC-14
Post Office Box 12233
Research Triangle Park, North Carolina 27709

Re: ROC Nomination Public Comment—Talc

Dear Dr. Jameson:

Enclosed are copies of two manuscripts describing our exposure estimation and epidemiologic study of workers at the Gouverneur Talc Company (GTC). These manuscripts report results from a study of GTC workers that was completed in 1995. A copy of the final report of that study was sent to NIEHS in November 2000. We recently submitted these manuscripts for consideration by the *American Journal of Industrial Medicine*, and we are hopeful that they will be accepted for publication by that journal.

As we indicated in our letter of November 2000 (copy attached), we do not believe that the results of this study support an interpretation that the talc dust in GTC operations is *per se* a lung carcinogen. Our reasons for this interpretation are explained in the attached letter, but they include our observations that excess lung cancer mortality was concentrated in short-term workers, lung cancer decedents had low estimated cumulative respirable dust exposure and no dose-response gradient for estimated respirable dust exposure and lung cancer mortality rate ratios was observed. In contrast, the study supports the body of evidence that talc exposure is associated with nonmalignant respiratory disease mortality.

Thank you for the opportunity to provide information about disease patterns among people exposed to talc. If you have any questions about these manuscripts, please call me any time.

Sincerely,

[redacted]

Colleen Beall, Dr.P.H.

/Enclosures (2)

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UAB SCHOOL OF PUBLIC HEALTH

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November 29, 2000

Dr. Mary S. Wolfe, Executive Secretary
NIEHS Mail Drop A3-07
111 TW Alexander Drive, Room A-329
Bldg 101 South Campus
Research Triangle Park, NC 27709

Re: 10th ROC Nominations: Solicitation of Public Comment—"Talc Containing Asbestiform Fibers"

In response to the referenced call for public comment, we are submitting herein written comments and are enclosing a copy of a report entitled, "Retrospective Follow-up Study of Mortality Patterns among Gouverneur Talc Company Workers." The report, which we issued in 1995, received peer review by several scientists. We are preparing two papers for publication based on the report and plan to submit the papers to a journal in January 2001.

The enclosed report describes the most recent analysis of mortality patterns among Gouverneur Talc Company (GTC) workers, a group that has been studied extensively over the past three decades. The report provides information related to the potential carcinogenicity of talc. We intend that this submission be considered by the National Toxicology Program (NTP) Board of Scientific Counselors' Subcommittee prior to the scheduled meeting on December 13-15, 2000.

Our study extended the follow-up period of previous investigations through the end of 1989 and incorporated several other improvements over previous research on GTC workers. In particular, our research:

- used, in addition to the United States general population, state and regional comparison groups;
- evaluated cause-specific mortality patterns by duration of employment and by time since first employment;
- estimated workers' quantitative exposure to total respirable dust; and
- analyzed lung cancer and nonmalignant respiratory disease mortality rates by estimated cumulative respirable dust exposure, using an internal referent group; these latter analyses reduce the possibility that results are due to confounding or observation bias.

Our study found that GTC workers, compared to the regional general population, had 2.3 times more than expected deaths from lung cancer (31 observed/13 expected deaths) and 2.2 times more than expected deaths from nonmalignant respiratory disease (28 observed/13 expected deaths). The lung cancer excess was concentrated in short-term employees and in underground

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miners. Millers, whose exposure to respriable dust was similar to that of underground miners, had only a small, statistically nonsignificant increase in lung cancer deaths. There was no, or an inverse, relation between cumulative respirable dust levels and lung cancer.

In contrast, an excess of nonmalignant respiratory disease deaths occurred both in short-term and in long-term workers and both in miners and in millers, and workers with cumulative dust exposure above the median had a higher mortality rate than other workers. In particular, decedents with pneumoconiosis or interstitial lung disease had median durations of employment and cumulative respirable dust exposure that were seven and 13 times higher, respectively, than the overall group of GTC workers.

We agree with the NTP that GTC workers clearly have increased mortality from lung cancer. However, several of our results argue against exposure to dust in GTC operations as the cause of the lung cancer excess:

- The lung cancer excess was concentrated in short-term workers, even when analyses were restricted to the employee subgroup with 20 or more years since hire (i.e., the subgroup with long induction time) (see our report, table III-8).
- The lung cancer excess was concentrated among underground miners (18 observed/4.1 expected, SMR=440, 95% CI=261-695), whereas millers, a group with estimated high exposure to dust, had an SMR for lung cancer of only 139 (7 observed/5.0 expected; 95% CI=56-287). Further, workers classified as unexposed to talc had a nonstatistically significant threefold increase in observed over expected lung cancer deaths (3 observed/0.97 expected, SMR=309, 95% CI=62-903) (see our report, table III-13).
- Lung cancer decedents had low estimated cumulative respirable dust exposure (median=297 mg/m^3-days) compared to the overall group of GTC workers (median=428 mg/m^3-days) (see our report, page 67 and table III-17), and cumulative respirable dust exposure levels were unrelated, or even inversely related, to lung cancer mortality rates (see our report, table III-16).

The lack of a dose-response gradient for estimated respirable dust exposure and lung cancer mortality rate ratios, along with the other results mentioned above, suggest that the overall increase in GTC workers is due, at least in part, to factors other than talc dust. The results do not support an interpretation that the talc dust in GTC operations is *per se* a lung carcinogen.

The NTP Review Group appears to have relied heavily on previous studies of GTC workers in determining if talc containing asbestiform particles is a human carcinogen. In reaching a final determination, we hope that the group will recognize that the various studies should not be considered as providing independent information on this topic. If, as several authors have suggested, the elevated lung cancer rate among GTC workers is due to an unidentified confounder (e.g., smoking, radon, other employment), the same confounder is likely to produce spurious results in all analyses of GTC employees, irrespective of the amount of follow-up time. Studies of truly independent groups (i.e., in Vermont and Norway), like studies of GTC workers,

have yielded inconclusive evidence that talc ore dust is a lung carcinogen. In particular, the Vermont study, like our GTC study, found that the respiratory cancer excess was restricted to miners and did not affect millers and suggests that some feature of the mine environment rather than talc ore dust is implicated.

Thank you for the opportunity to add to the information about disease patterns among people exposed to talc being considered by the NTP.

Yours sincerely,

[redacted]

Elizabeth Delzell, SD

[redacted]

Kent Oestenstad, PhD

Please see R.T. Vanderbilt comments of April 11, 2001, for submitted manuscripts referred to in Dr. Colleen Beall's cover letter.

National Toxicology Program
Report on Carcinogens