of Upstate New York where the TMX mine is located and where many of the TMX workers were previously employed.[2] These mineralogical analyses are improtant when interpreting the toxicity of TMX talc because previous studies of workers exposed to talc from other Upstate New York mines also found an excess in mortality due to lung cancer and non-malignant respiratory disease,[2,3] and other studies of workers exposed to anthophyllite and tremolite have demonstrated similar findings.[4] Thus, the NIOSH conclusions are not based on the results of the cohort mortality study alone, but also on environmental sampling and on the corroboration of findings at TMX with previous reports.

Several problems in the TOMA analysis appear to account for the difference between the TOMA and NIOSH conclusions. First, the TOMA study performed no analysis of mortality by latency interval. Instead, the TOMA study allows workers to enter the cohort as late as December 31, 1977. In the absence of a proper analysis of risk by latency, the possibility arises that a number of recently hired workers are included in the TOMA study group, and that their low rate of cancer mortality may have masked any excess risk that truly existed among workers who had experienced an adequate observation period, i.e., who had first been employed prior to 1960.

Second, the distinction made in the TOMA study between previously employed and not previously employed workers overlooks several possibly confounding factors. To address the possible influence of exposures from previous jobs, the TOMA study divided the cohort into those with *any known* work history prior to employment at TMX and those with *no* known previous work history. This exercise yields a sub-cohort of 540 workers with previous employment and another of 115 workers with no previous employment. When cause-specific mortality of the two sub-cohorts is examined, the risks associated with the first (N=540) are unusually high for almost every cause, while those of the second (N=115) are unusually low. The TOMA investigators suggest that this difference may reflect hazardous prior exposures, but in fact, it appears to be a consequence of selection biases inherent in the definition of the subcohorts. These selection biases include differences in the length of the follow-up period (i.e., those with previous employment probably have a much longer time since first exposure), and differences in the percentage of more recently hired workers (i.e., there is probably a much higher percentage of more recently hired workers in the group with no previous employment, a difference which exaggerates the healthy worker effect). Furthermore, the size of the population with no previous employment is extremely small (23 total deaths, 3 cancer deaths). Any mortality analysis based on such a small cohort with generally short latency is not likely to be very informative.

Third, the TOMA study does not calculate the relative risk of lung cancer by "dose." The conclusion reached in the TOMA study that there is ". . . an inverse dose response, i.e., higher risks of lung cancer with less occupational exposure . . ." is supported by an analysis which simply counts the number of observed deaths (and not the expected number of deaths) in each category of years employed. Such an analysis is not very meaningful. The same comment can be made about the TOMA latency analysis which employs the same procedure. In addition, TOMA's conclusions regarding the "negative" effect of dose-response and latency ignore the fact that many TMX workers had previous employment in other neighboring talc companies where the talc has been shown to be basically the same as that at TMX.

In summary, the TOMA report fails to address adequately the question of whether or not there is an increased risk from lung cancer specifically associated with working at the TMX facility. In fact, at this time, it is not possible to answer this question based on epidemiologic data alone, because the population available for study is small, the follow-up period is relatively short (long latency diseases associated with employment at this company cannot be adequately addressed), data on smoking are lacking, and previous exposures in other neighboring talc mines and mills represent a confounding factor. In addition, in order to conclude that the talc from TMX is *not* carcinogenic as stated by TOMA would require: (1) a negative study based on a cohort of sufficient size that also has sufficient latency; (2) a demonstration that the talcs from the TMX mine are different from other talcs in Upstate New York in their content of tremolite, anthophyllite and other contaminants; or (3) that other mortality studies of Upstate New York talc workers incorrectly attributed increased lung cancer mortality to talc exposures. The TOMA study does not adequately address any of these considerations.

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Authors' Response

The NIOSH study of mortality among TMX workers purports to show that the exposure agent was talc containing significant quantities of asbestos.[1] However, the definition of asbestos and the methods for identification used by NIOSH and "independent laboratories" to support this finding are unacceptable to mineral scientists since these methods cannot

positively identify asbestiform particles, nor can they distinguish between the asbestiform and nonasbestiform varieties of the minerals listed in asbestos health standards. Other independent laboratories, as well as the Bureau of Mines, would seriously disagree with the definition and methodology used by NIOSH to identify and count "asbestos" in complex silicate mineral mixtures.[2-5] Using methods generally accepted by mineral scientists, both the Bureau of Mines and others* have found TMX talc to be free of significant asbestos concentrations.[2,6]

Furthermore, NIOSH's claim is incorrect that talc ore from the TMX mine was substantially the same historically as that of other mines in the Gouverneur Talc District of Upstate New York. Its claim is based upon analytical results of 10 atmospheric samples taken during the grinding of one type of ore in a separate mill at TMX. The mineralogical composition of the St. Lawrence County talc belt varies considerably.[7,8] Over the many years of talc production in the district, selective mining has resulted in the production of widely different industrial talc mixtures at various grinding sites.[9-11]

NIOSH included in its cohort workers with employment of *any* duration at TMX. Of the nine deaths due to bronchogenic cancer in the NIOSH cohort, four were employed less than one year (one was employed for eight days, another 17 days). This contrasts with the minimum of one year employment period specified in the NIOSH studies of Vermont talc workers exposed to "nonasbestiform" talc[5] and Homestake gold mining workers exposed to "asbestiform" minerals.[12] Even in the references study of asbestos miners in Finland[13] where exposures to 100% anthophyllite asbestos were involved, only workers with more than three months employment were included in the cohort. If the study design had not included workers with less than one year exposure, the increase in lung cancer reported by NIOSH would not have been statistically significant. This would be the case even if one ignored the potential effects of prior work history, absence of dose-response relationship, the use of United States mortality rates rather than New York State rates, early exposure levels and the heavy smoking patterns seen in the mining industry.

Brown, et al, observe that several problems with the TOMA analysis appear to account for the discrepancy between the findings of the two studies:

(1) *Latency:* NIOSH ignores the finding of the TOMA latency analysis, which demonstrated the inconsistency between the average latency period (19.9 years) of the TMX bronchogenic cancer cases and those seen in other studies (36.5 years). Additionally, NIOSH's own latency analysis (Table 31) includes four workers in the 20-28 year employment period who worked less than one year at TMX. Excluding these would eliminate any significant increase in SMR with increasing latency.

(2) *Cohort selection biases:* NIOSH's concerns deserve analysis; however, because of an historical management policy to hire experienced workers, it is doubtful that the cohort contains a higher percentage of more recently hired workers with no prior work experience. In addition, the single largest infusion of new hires other than at plant opening came in 1974 when workers from a nearby talc mine acquired by the Company were added to the TMX work force. We couldn't agree more with NIOSH that the subcohort of workers with "pure" TMX exposure is small. In fact, small cohort size is a problem of both the NIOSH study (N = 398) and TOMA's (N = 655), a point repeatedly made in the TOMA paper. The rationale for subdividing the cohort remains sound. Moreover, as the TOMA document notes, even taking the cohort as a whole, the increase in bronchogenic cancer cases can be explained by a smoking effect.

(3) *Cancer risk by "dose":* As stated earlier, it *is* important that so many of the lung cancer cases were workers who had been employed less than one year. Similarly, one cannot overlook the fact that only one miller contracted lung cancer (millers' dust exposure historically has been greater than that of miners). The latter finding was also noted in the Vermont study, which led the authors to conclude that agents other than talc (e.g., radon daughters), "either alone or in combination with talc dust, affect mine workers."

We agree with NIOSH that at this time it is not possible to state definitively *based on epidemiologic evidence alone* that there is an increased lung cancer risk from TMX employment. However, our review of the data strongly suggests there is not, and this has been confirmed both in animal studies and on-going medical surveillance examinations of TMX workers. For NIOSH to recommend application of the asbestos standard to this work force is unwarranted based on current evidence.

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* Evaluation of six talc samples from Duncan Enterprises by U.S. Bureau of Mines, Particulate Mineralogy Unit, College Park, Md., Aug. 26, 1977, and Mine Safety and Health Administration dust sampling results, Gouverneur, N.Y., July, 1979.

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Unidentified Risk Factor?

To the Editor: The significantly high SMR obtained for cerebrovascular disease in copper and zinc refinery workers as studied by Dr. Logue et al (*JOM* 24:398-408, 1982) is certainly of great interest and, as is pointed out in the paper, reproduces findings from two independent and methodologically different Swedish studies from the same primary copper smelter.[1,2] The question is, of course, what specific agent or process might be responsible – or has uncontrolled confounding resulted in a spurious association as discussed in the paper? The reappearance of this unexpected association in this new study from another continent makes it likely, however, that a particular risk factor not yet identified is operating.

We speculated as to the possibility that copper exposure itself would be of etiological importance, and therefore studied a small secondary copper smelter (producing copper tubes and various products in copper alloys) with particular attention to any possible excess of cerebrovascular deaths in the workforce. This was a small scale study, however, and since it came out negative we hesitated to publish the data. In view of the finding of excess cerebrovascular disorders in U.S. refinery workers, there is perhaps a reason to indicate briefly the existence of our study and present some of the data.

A study of the causes of deaths in the small parish surrounding the smelter, Gusum, in southeastern Sweden, yielded data shown in Table 1. The finding of a numerical excess of cerebrovascular deaths in the parish, which except for the smelter works is quite rural in character, was further delineated through a case control approach considering occupational titles of the individuals (lists with cases and controls were sent to the factory for identification of employment). There was no indication of excess risk of cerebrovascular disease for workers in the copper smelter (Table 2).

Our small scale study does certainly not rule out copper exposure itself as a risk factor for cerebrovascular disease but tends to decrease the likelihood of such a relation.

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Table 1 – Mortality Analysis on Cerebrovascular Deaths (ICD 1965: 430-438) During 1960-79 Among Men in the Parish as Compared to the National Average.

Age	Observed	Expected	O/E
45-64	6	3.92	1.53
65-74	8	7.80	1.03
75-	25	13.36	1.87
All	39	24.24	1.61

Table 2 – Case-Control Study on Cerebrovascular Deaths with Regard to Employment in Copper Smelter.*

Age	Case/contr	Employed	Non-employed
45-64	Ca	3	3
	Co	15	19
65-74	Ca	1	7
	Co	17	33
75-	Ca	5	20
	Co	12	57
All	Ca	9	30
	Co	44	109

* Controls are other deaths registered before and after each case in the parish register.
Crude rate ratio = 0.74
$x^2(1) = 0.089$ (Mantel-Haenszel)
Mantel-Haenszel rate ratio = 0.88
Approx 95% conf. interv. 0.4-2.1