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Exposure to airborne amphibole structures and health risks: Libby, Montana

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Abstract

Libby, Montana is the site of a large vermiculite deposit that was mined between 1920 and 1990 to extract vermiculite for commercial applications such as insulation, gardening products, and construction materials. The Libby vermiculite deposit also contains amphibole minerals including tremolite, actinolite, richterite, and winchite. Historically, Libby mine workers experienced high exposures to amphibole structures, and, as a group, have experienced the health consequences of those occupational exposures. It has been suggested that Libby residents also have been and continue to be exposed to amphibole structures released during the vermiculite mining operations and therefore are at increased risk for disease. The Agency for Toxic Substance and Disease Registry (ATSDR) conducted two epidemiological-type studies of residents living in Libby and the surrounding areas to assess these risks. The Environmental Protection Agency (EPA) collected and analyzed exposure data in Libby and used those data to project risks of asbestos-associated disease for Libby residents. The EPA has placed the Libby Asbestos Site, which includes the mine and the town of Libby, on its National Priority List of hazardous waste sites in need of clean up. This article presents a review of the exposure studies conducted in Libby and an analysis of health risks based on the data collected in those studies. Libby mine workers have experienced elevated levels of asbestos-associated disease as a consequence of their occupational exposures to amphibole structures. Libby residents' exposures typically are substantially lower than mine workers' historical exposures, and the health risk projections for residents are, accordingly, substantially lower.

Keywords: Libby; Montana; Vermiculite; Amphibole minerals; Asbestos; Asbestos-associated disease

1. Introduction

Libby, Montana gained the attention of the U.S. government health agencies in 1999 when the Seattle Post Intelligencer ran an article by Andrew Schneider titled "A town left to die". The article associated high rates of respiratory disease in Libby with exposure to amphibole particles released into the air from the vermiculite mine located in Libby.

Vermiculite is the mineralogical name given to hydrated laminar magnesium–aluminum–iron silicate that resembles mica in appearance. When subjected to heat, vermiculite has the unusual property of exfoliating or expanding into worm-like pieces. This characteristic of exfoliation is the basis for commercial use of vermiculite in applications such as insulation, gardening products, and construction materials.

Commercially useful vermiculite is found in Australia, Brazil, China, Kenya, South Africa, the U.S., and Zimbabwe. In the U.S., vermiculite is mined at Enoree, South Carolina and Libby, Montana. The Libby mine, which operated from 1920 to 1990, may have produced as much as 80% of the world's supply of vermiculite.

The Libby vermiculite deposit contains amphibole minerals. It has been suggested that the amphibole component of the ore deposits at the vermiculite mine has unique characteristics that make its potency for asbestos-associated disease different than other asbestos minerals. "Libby Asbestos" (LA), a term coined by the United States Environmental Protection Agency (EPA) and the Agency for Toxic Substance Disease Registry (ATSDR), is a collection

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of amphibole minerals including tremolite, actinolite, anthophylite, richterite, and winchite. LA is a combination of asbestiform structures (i.e., fibers) and non-asbestiform structures known also as cleavage fragments.

High-level exposure to LA has been associated with various diseases including lung cancer, mesothelioma, asbestosis, and other non-malignant respiratory diseases (McDonald et al., 1986; Amandus et al., 1987a; Amandus and Wheeler, 1987b). This article presents a review of the exposure studies conducted in Libby and an analysis of health risk based on the data collected in those studies. Libby mine workers have experienced elevated levels of asbestos-associated disease as a consequence of their occupational exposures to amphibole particles. Libby residents' exposures typically are substantially lower than mine workers' historical exposures and the health risk projections for residents are, accordingly, substantially lower.

2. Chronology of health studies and regulatory actions in Libby

The vermiculite mining operation in Libby between 1920 and 1990 consisted of ore extraction, processing, and shipping. Until the 1960s, mine workers often were exposed to high levels of LA, which co-existed with the vermiculite ore. In the mid-1980s, W.R. Grace and the National Institute for Occupational Safety and Health (NIOSH) conducted separate epidemiology studies of mine workers to assess heath risks associated with exposure to LA in vermiculite mining (McDonald et al., 1986; Amandus et al., 1987a; Amandus and Wheeler, 1987b). ATSDR and EPA initiated studies of respiratory disease among Libby residents in 1999. In 2000, ATSDR released a report describing the results of its study of asbestosis mortality in Libby (ATSDR, 2000). The report stated that the asbestosis mortality rate in Libby was 40–60 times greater than the national average asbestosis mortality rate. During the summer of 2000, ATSDR initiated a medical testing program and Screening Study. ATSDR's report on the Screening Study, released in 2001, stated that Libby residents experienced a high rate of pleural abnormalities (ATSDR, 2002b). Also in 2001, the EPA summarized an exposure analysis it had conducted in Libby stating that exposure to asbestos in Libby constituted an "imminent and substantial endangerment to public health" (Weis, 2001). In 2002, EPA placed Libby on the National Priorities List of the Superfund Program, which established it as a hazardous waste site requiring clean-up. Also in 2002, ATSDR revised its asbestosis mortality study, updated its Screening Study, reported on a pilot study of environmental cases of pleural abnormalities, and issued a Public Health Assessment for vermiculite (ATSDR, 2002a; ATSDR, 2002b; ATSDR, 2002c; ATSDR, 2002d). The studies addressing the rate of pleural abnormalities among Libby residents were summarized and published with comments in Environmental Health Perspectives (Peipins et al., 2003a,b; Price, 2004). The remainder of this article contains a review of the mine worker and Libby resident studies and regulatory actions concerning Libby. Included are re-analyses of data in order to evaluate concerns about the health risk of low-level environmental exposure to LA.

3. Morphology characterization of LA

LA is a collection of amphibole minerals that have been identified as tremolite, actinolite, soda tremolite, richterite, and winchite (Meeker et al., 2001). A typical sample of LA also contains acicular cleavage fragments. Because LA is a mixture of pure fibers and acicular morphologies, in the remainder of this report LA particles are referred to as structures rather than fibers. The toxicities of the mineral components of LA have not been thoroughly studied. Cleavage fragments, in particular, are at the center of a controversy concerning their toxicity for asbestos-associated disease. Currently, The Occupational Safety and Health Administration (OSHA), excludes cleavage fragments from the mineral fibers it regulates under its asbestos exposure standard (57 FR 24310). The relative toxicity of cleavage fragments, which tend to be thicker and shorter than fibers, although uncertain, is generally considered to be less than the asbestiform analogue (Ilgren, 2004; Davis et al., 1991; Wylie et al., 1993; ATS, 1990). Notwithstanding the specific toxicity uncertainties associated with cleavage fragments, it is generally accepted that inhalation of long, thin fibers (longer than 5 μm with diameters less than 0.50 μm) have greater potential to cause disease than shorter, thicker fibers (ATSDR, 2003a; EPA, 2003).

Table 1 contains a summary of data concerning the size distribution of LA. Amandus et al. (1987a) summarized lengths and widths separately based on light microscopy inspection of 599 LA structures collected in air samples. Amandus reported results only for structures longer than 5 μm and thicker than 0.45 μm. Seventy four percent (74%) of the structures were longer than 10 μm, 11% were longer than 40 μm, and 93% had diameters between 0.45 and 0.90 μm. McDonald et al. (1986) provides preliminary results of an electron microscopy study to characterize the structure size distribution of LA conducted by the Institute of Occupational Health and Safety at McGill University. McDonald's results indicate that 62% of LA structures were longer than 5 μm. Additional results from McGill based on three air samples confirm McDonald's result (McGill University, 1983). Ten percent (10%) of the structures were longer than 20 μm and 73% were thinner than 0.50 μm. The McGill data also provides information about the two-dimensional distribution of structures. Focusing on structures no thicker than 0.50 μm, 38.9% were longer than 5 μm; 13.1% were longer than 10 μm; and 2.7% were longer than 20 μm.

ADL (1983) used electron microscopy to determine the percentage of structures typically counted by light micros-

Table 1
Fiber sizes: asbestos from the Libby vermiculite mine[a]

Phase contrast microscopy (PCM)		Transmission electron microscopy (TEM)					
Amandus et al., 1987a,b		McDonald et al., 1986		McGill University, 1983[b]		ADL, 1983	
Length	Percent	Length	Percent (%)	Number	Percent (%)	Number	Percent (%)
<5.0	N/A	<5.0	38	80	36	N/A	N/A
5–10	27%	5–10		82	37	93	46
10–20	37%	10–20	62	38	17	85	42
20–40	26%	20–40		17	8	21	10
>40	11%	>40		4	2	2	1
Width		Width					
<0.25	N/A	<0.25		86	39	56	28
0.25–0.45	N/A	0.25–0.50		76	34	95	47
0.45–0.90	93%	0.50–0.90	100	33	15	37	18
0.90–1.25	5%	0.90–1.25		10	5	10	5
1.25–2.00	2%	1.25–2.00		16	7	3	1
>2.00		>2.00	0	0	0	0	0

[a] The samples underlying these data were not collected according to a formal statistical design. Therefore, the data are not necessarily representative of LA and should be interpreted only as information about the size distribution of LA, but not as a formal characterization of the size distribution.
[b] Width frequencies are approximations.

copy that were tremolite. The results, based on analysis of two samples, indicate that 50–75% of optically visible structures were tremolite. ADL also reported the structure size distribution. However, the ADL results cannot be compared to the McGill results because ADL did not include counts of structures shorter than 5 μm.

Recently, air sampling was conducted in Libby to determine the potential LA exposures of Libby residents. Brattin (2002) and RJ Lee Group (2002) discuss the structure size distribution of these data. The air samples were collected: (1) at the location of a former export/screening plant; (2) in residential and commercial properties; and (3) from attics with vermiculite attic insulation (Brattin, 2002). Based on average length, width, and aspect ratio, Brattin (2002) concludes that current samples of LA have the same structure size distribution as samples collected when the mine was operating. The RJ Lee Group (2002) analysis indicates that a high percentage of the current airborne structures, possibly 80%, are cleavage fragments.

Information about LA structure type and size distributions is important in estimating exposure and risk for Libby residents. The scientific literature indicates that cleavage fragments are most likely less carcinogenic than asbestos fibers, and short structures (e.g., lengths less than 5 μm) are less carcinogenic than long, thin fibers (Ilgren, 2004; ATSDR, 2003b; EPA, 2003; Wylie et al., 1993; OSHA, 1992). Based on available data, LA appears to consist of amphibole minerals in many size ranges including long, thin amphibole structures. Therefore, environmental exposures, if sufficiently high, could increase the risk of disease for Libby residents.

4. Epidemiology studies of Libby mine workers

Two retrospective epidemiological studies of Libby mine workers have been conducted (McDonald et al., 1986; Amandus et al., 1987a; Amandus and Wheeler, 1987b) to assess the risk of asbestos-associated disease from LA. Recently, McDonald reported results on an update of his study that included the vital status of the worker cohort through 1999 (McDonald, 2001; McDonald et al., 2002, 2004).

The Amandus and McDonald studies differ in three respects that may affect interpretation of the results. First, McDonald's cohort consisted of 406 workers versus 575 workers in the Amandus study. Second, McDonald's follow-up period continued through December 31, 1999, which accounted for 285 deaths among the 406 cohort members. Amandus followed workers through December 31, 1981, which accounted for 161 deaths among 575 cohort members. Finally, McDonald's external reference group for standard mortality ratio (SMR) calculations was white males in Montana. Amandus used white males in the U.S as the external reference group for SMR calculations.

SMRs indicated excess lung cancer and excess nonmalignant respiratory disease (NMRD) in both studies. The SMRs from the two studies are not directly comparable because the two studies used different external reference groups to determine the numbers of expected cases. Exposure–response analyses of these data restricted to subjects with latency greater than 20 years (i.e., time since hire greater than 20 years), discussed below, show the excess in lung cancer occurs primarily at the higher exposure levels.

Mesothelioma cases were observed in both studies. Amandus recorded 2 cases. The proportional mortality ratio (PMR) for the Amandus cohort was 1.2%. Based only on deaths for workers with latency greater than 20 years, the PMR was 2.2%. Amandus stated that the minimum exposure for the mesothelioma cases was 300 f-yr/cc. McDonald recorded 12 mesotheliomas for a PMR equal to 4.2%. The average exposure for these 12 cases was 48.1 f-yr/cc.

4.1. Lung cancer

This section describes an investigation of the relationship between LA exposure and lung cancer risk. The data reported by Amandus and Wheeler (1987b) and McDonald et al. (McDonald et al., 1986; McDonald, 2001; McDonald et al., 2002) have been used to re-estimate the relationship between lung cancer risk and exposure, and to expand upon the interpretation of the results that the authors reported.

4.1.1. Lung cancer risk models

McDonald et al. (1986) and Amandus and Wheeler (1987b) use a linear risk model for lung cancer identical to the model employed by EPA. In this model, SMR, which is the ratio of observed lung cancer cases (O) in the cohort to the expected number of cases (E) based on an appropriate reference population, is represented as a linear function of lifetime cumulative exposure (f-yr/cc). E, also referred to as the background rate of lung cancer, varies with age, sex, and smoking history. The model may have one or two parameters. The principal parameter is K_L, referred to as the "slope" parameter, which measures the potency of asbestos for lung cancer. The role of K_L is shown in the single parameter model Eq. (1):

$$\mathrm{SMR} = 1 + K_L \cdot (\text{f-yr/cc}). \tag{1}$$

In this one-parameter version of the model, if the asbestos exposure level is zero, SMR is equal to 1.0. Using Eq. (1) and the definition of SMR, the incremental number of lung cancer cases associated with exposure to asbestos is: $I = E \cdot K_L \cdot (\text{f-yr/cc})$.

The two-parameter version of this model allows for differences between the study cohort and the external reference group in lung cancer risk factors other than asbestos exposure. The two-parameter model may be stated either as:

$$\mathrm{SMR} = \alpha + K_L \cdot (\text{f-yr/cc}); \tag{2}$$

or

$$\mathrm{SMR} = \alpha \cdot [1 + K_L \cdot (\text{f-yr/cc})]. \tag{3}$$

In both forms of the model, α measures the difference in lung cancer mortality between the internal control group (i.e., study cohort members who were not exposed to asbestos) and the external reference group. For example, if the only lung cancer risk factor in addition to asbestos exposure were smoking, α measures the difference in smoking effect between the study cohort and the external reference group.

In EPA (1986), the relationship between lung cancer and exposure was analyzed using Eq. (2) for a number of different epidemiology studies.[1] EPA used the results to develop the lung cancer component of the quantitative risk assessment published in its Integrated Risk Information System (IRIS).[2] Berman and Crump (2003), working with EPA's Superfund Program, updated the asbestos lung cancer risk analysis using Eq. (3).

The Amandus and McDonald data, which are displayed in Fig. 1, were used to estimate each of the three alternative models. Fig. 1 includes 99% confidence limits for the SMRs for each exposure category. The plots show that although SMR has an increasing trend with exposure, the increase is determined principally by the highest exposure group. In addition, the increase in lung cancer due to asbestos exposure is not statistically significant for the low exposure categories. The parameter estimates for the three models are summarized in Table 2 and discussed below.

4.1.2. Amandus study

As indicated in Table 2, each of the three models provides an adequate description of the Amandus data (i.e., deviance p-value greater than 0.05). Based on the value of α in Models 2 and 3, which has a value less than 1.0, the internal control group appears to have fewer lung cancer cases than the external reference group. The range of asbestos potency for lung cancer, K_L, based on the Amandus data is 0.006–0.0077 $(\text{f-yr/cc})^{-1}$. These values are less than, but near, the asbestos potency value EPA currently employs in its asbestos risk assessment, 0.01 $(\text{f-yr/cc})^{-1}$ (EPA, 1986).

The parameter estimates obtained with the Amandus data also were used to provide additional interpretation of the relationship between LA exposure and lung cancer. The exposure level required to double lung cancer risk versus the external reference group and the incremental risk of lung cancer associated with LA exposure to 25 f-yr/cc were calculated. The "risk-doubling" exposures all exceed 150 f-yr/cc. The incremental risk associated with 25 f-yr/cc is less than 0.20.

4.1.3. McDonald study

The results in Table 2 indicate that EPA's primary lung cancer model Eq. (1) is not consistent with McDonald's data (p-value less than 0.05). The results for Models 2 and 3 indicate an excess of lung cancer cases among the internal controls relative to the external reference group. McDonald used Montana white males as the external reference group. Models 2 and 3 provide an adequate representation of the data. It is not possible to differentiate statistically between Model 2 and Model 3, however, Model 1 does not fit the data. The results for models 2 and 3 suggest a potency value less than 0.006, which is less than EPA's potency value of 0.01 used to develop its IRIS risk assessment in 1986. The "risk doubling" exposures calculated from these models are not meaningful because the

[1] The Libby mine worker data were not included in EPA's 1986 report.

[2] The quantitative risk relationship in the IRIS asbestos file addresses total cancer risk (i.e., the sum of lung cancer and mesothelioma risks).

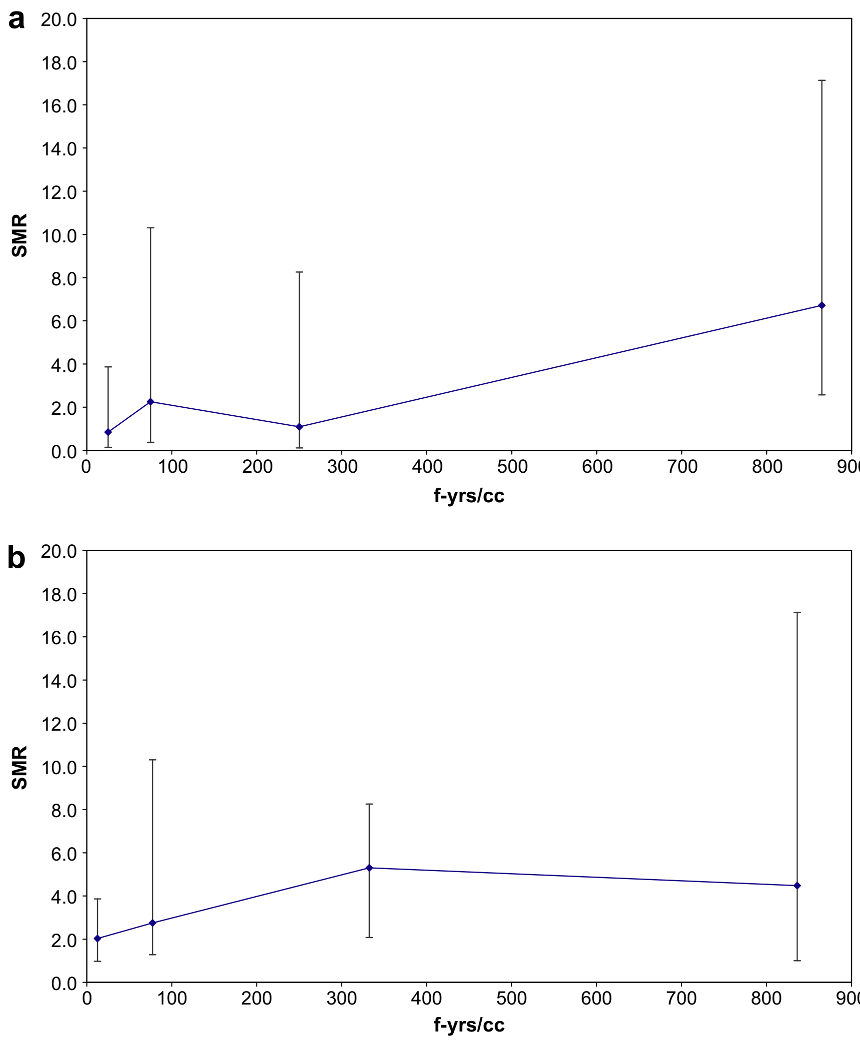

Fig. 1. Lung cancer SMR and 99% confidence limits: (a) Libby Miners (Amandus, 1987b) and (b) Libby Miners (McDonald, 2001).

internal controls have a lung cancer risk greater than two times the reference group risk. The incremental lung cancer risk associated with exposure to 25 f-yr/cc is less than 0.14.

4.1.4. Lung cancer summary of Libby mine worker studies

Based on a linear exposure–response assumption, data published by Amandus and McDonald estimate LA unit risk for lung cancer between 0.0025 $(\text{f-yr/cc})^{-1}$ and 0.0077 $(\text{f-yr/cc})^{-1}$. McDonald et al. (2004) includes an estimate of Model 1 based on miner cohort follow-up data through 1999. The estimate of unit risk for these data was 0.0036.[3] These values are less than the unit risk employed by EPA in its IRIS risk assessment. Therefore, following the EPA risk assessment approach, LA is not more potent for lung cancer than other asbestiform amphiboles.

[3] This unit risk factor was statistically different from zero (p-value = 0.02). McDonald applied Poisson regression to estimate the unit risk factor. The data used by McDonald were not available for re-analysis.

4.2. Mesothelioma

Data concerning mesothelioma reported in the two epidemiology studies are insufficient to estimate risk models that could be used to assess the relative potency of LA for mesothelioma. Amandus and McDonald report mesotheliomas among the study cohorts. Amandus and Wheeler (1987b) found two mesothelioma cases for a proportional mortality ratio (PMR) of 1.2%. McDonald (McDonald, 2001; McDonald et al., 2002, 2004) found 12 mesotheliomas (PMR = 4.2%). As expected, due to the relatively high exposure levels experienced by mine workers, these PMRs are substantially larger than the U.S. male PMR for mesothelioma. Based on SEER data for the year 2000, the estimated U.S. PMR for male mesothelioma is approximately 0.2%.

Amandus and Wheeler (1987b) stated that both cases he reported had exposures that exceeded 300 f-yr/cc. Cumulative exposure for 11 of the 12 mesotheliomas reported by McDonald had exposures exceeding 11.7 f-yr/cc. McDonald reports exposure for the remaining mesothelioma case as a range between zero and 8.6 f-yr/cc.

Table 2
SMR versus exposure for Libby vermiculite miners: summary of regression modeling

Study	Model	α	Slope (K_L)	Deviance p-value	Exposure level for SMR = 2.0 (f-yr/cc)	Contribution to SMR due to asbestos exposure of 25 f-yr/cc
Amandus et al. (1987a,b)	Model 1	1.00	0.0058	0.22	173	0.14
Amandus et al. (1987a,b)	Model 2	0.85	0.0060	0.50	192	0.15
Amandus et al. (1987a,b)	Model 3	0.81	0.0077	0.50	155	0.19
McDonald (2001)	Model 1	1.00	0.0108	<0.01	93	0.27
McDonald (2001)	Model 2	2.15	0.0055	0.51	N/A	0.14
McDonald (2001)	Model 3	2.16	0.0025	0.51	N/A	0.06

Note. Model 1—Eq. (1): $\text{SMR} = 1 + K_L \cdot (\text{f-yr/cc})$.
Model 2—Eq. (2): $\text{SMR} = \alpha + K_L \cdot (\text{f-yr/cc})$.
Model 3—Eq. (3): $\text{SMR} = \alpha \cdot [1 + K_L \cdot (\text{f-yr/cc})]$.
p-value: A p-value greater than 0.05 indicates an adequate fit to the data.
N/A: The data indicate that lung cancer incidence for the internal controls was more than double the incidence for external controls, therefore the calculation provides no information.

The range of cumulative exposures for the mesothelioma cases is particularly significant for assessing mesothelioma risk for Libby residents. EPA has estimated lifetime cumulative exposures to LA for Libby residents for various activities. The maximum of these lifetime cumulative exposures is 0.04 f-yr/cc (Ref. Table 8 and Weis, 2001, 2002).[4] No broadly accepted threshold exposure limit for mesothelioma exists that could be used to evaluate the significance of exposures of 0.04 f-yr/cc.[5] However, Price and Ware (2004), based on mesothelioma incidence trends in the U.S., argue that such a threshold exists, and, in addition, suggest a background risk level for mesothelioma (i.e., the risk of mesothelioma absent exposure to asbestos). The lowest exposure among the Libby mine worker mesothelioma cases suggested by the McDonald data, the midpoint of the exposure range for the lowest exposure group, 4.3 f-yr/cc, is a candidate for the mesothelioma exposure threshold for LA. However, the size of the Libby mine worker cohort is insufficient to adopt this value for all risk management purposes. Ambient exposure for an 80-year lifetime would be an extremely conservative lower bound for the mesothelioma exposure threshold. If the long-term average ambient concentration of asbestos were 0.005 f/cc, lifetime cumulative exposure would be 0.40, 10 times greater than the maximum lifetime cumulative exposure projected for a Libby resident (Ref. Table 8). In addition, if EPA's current risk assessment methodology (EPA, 1986) were used to estimate lifetime risk of mesothelioma for the maximally exposed resident of Libby, the risk would be 1.1×10^{-4}, less than the background risk of mesothelioma estimated by Price and Ware (2004).[6] Therefore, by any reasonable assessment, the likelihood of mesothelioma for the maximally exposed resident of Libby would be negligible.

5. ATSDR health consultation

In December 2000, ATSDR, in cooperation with the Montana DPHHS, released an analysis of mortality in Libby–Montana for the years 1979–1998 (ATSDR, 2000). The analysis, based on a review of death certificate data, was conducted to develop information about mortality potentially associated with asbestos exposure in Libby. Six geographic boundaries with increasing areas were used for the analysis. The smallest area was Libby city limits—1.1 square miles. This area was increased in steps to the final area, central Lincoln County—a 314-square mile circular area with a 10-mile radius centered in downtown Libby. Each decedent was classified into an area and SMRs were calculated for each area. The study population initially consisted of 419 decedents. ATSDR updated the study (ATSDR, 2002a) by adding death certificates for decedents that would have been included in the initial analysis if they had been discovered during the initial search. The revision analyzed data for 542 decedents and provided a clearer picture of causes of mortality than the initial report.

The initial report stated that mortality due to asbestosis in Libby was 40–80 times greater than expected. The report failed to mention that virtually all the asbestosis deaths, as well as other deaths associated with asbestos, were found

[4] Air samples were analyzed by electron microscopy. A structure was included in the count only if it was longer than 5 μm, thicker than 0.25 μm, had an aspect ratio of at least 3:1, and was asbestos. This counting protocol has the same structure dimension criteria as the standard measurement method based on Phase Contrast Microscopy (PCM) used by OSHA. The method, which includes only asbestos structures, is referred to as Phase Contrast Microscopy Equivalent (PCME).

[5] "Threshold," as it is used in this article, means an exposure level where the probability of incremental mesotheliomas is small enough to characterize the risk as negligible.

[6] Price and Ware (2004) estimate background lifetime mesothelioma risk between 3 and 4 per 10,000 (3.4×10^{-4}). Mesothelioma risk based on the EPA method was calculated from Table 7 in EPA (1986). The table evaluates risk based on lifetime average daily exposure equal to 0.01 f/cc. Exposure for the maximally exposed Libby resident is 0.04 f-yr/cc divided by 70 years (assumed lifetime for these calculations). The result, 5.7×10^{-4}, was applied to the first row in the table for males (exposure beginning at birth and continuing for a lifetime). The risk, 1.1×10^{-4}, was calculated as $(5.7 \times 10^{-4}/0.01) \times 192.8 \times 10^{-5}$.

among former workers at the Libby mine. This information is critical input for risk management decisions and public policy because it indicates the excess mortality due to asbestos exposure occurred in an occupational group that experienced extremely high asbestos exposures. Such a result is not unexpected. Absent this information, a reader of the ATSDR report would be likely to conclude that all residents of Libby, not only the group of mine workers who experienced high levels of occupational exposure to asbestos, were at increased mortality risk based simply on being a resident of Libby. A discussion of ATSDR's principal results follows.

5.1. Asbestosis

Asbestosis mortality in Libby was 40 times greater than expected in comparison to the state of Montana reference population, and 80 times greater than expected when compared to the U.S. reference population. These results were based on 12 asbestosis deaths; 11 were males previously employed in the Libby mine. The remaining one female was a household contact of a former mine worker who was employed at the mine for 20 years (ATSDR, 2001). The high multiples of asbestosis deaths relative to the number of asbestosis deaths expected in the reference populations are misleading. The mine workers would have experienced high exposures to asbestos over extended time periods whereas the average inhabitant, whether of Montana or the U.S., would most likely have only background asbestos exposure. It is unclear how the household contact would have experienced exposures high enough to cause asbestosis. A threshold exposure for asbestosis between 25 f-yr/cc and 100 f-yr/cc has been suggested (Churg and Green, 1998; EPA, 1986). Therefore, the correct interpretation of the asbestosis mortality rates reported by ATSDR should be—a typical resident of Libby or its surrounding areas who was not a mine worker would not be at increased risk of death due to asbestosis.

5.2. Lung cancer

The ATSDR results show a statistically significant excess of lung cancer for males relative to the male Montana population, but not relative to the male U.S. population. Females showed no statistically significant excesses relative to either reference group.

The statistically significant excess for males would be misleading if it were interpreted as a characterization of lung cancer for typical Libby residents for a number of reasons. First, the primary cause of lung cancer is smoking and no data were analyzed to adjust for smoking. Second, females, because they typically did not work at the mine, would provide the best information on lung cancer risk for Libby residents with environmental exposure to LA. Females showed no statistically significant excess of lung cancer relative to either of the reference populations. Third, 21 lung cancer decedents were formerly mine employees. These decedents would have had occupational exposures to LA. To properly judge the impact of asbestos-associated lung cancer risk for Libby residents, it would be appropriate to exclude these workers from the risk calculations. Although the ATSDR report does not indicate the number of males and females among these 21 decedents, it is reasonable to expect that they were all male. Assume that all were male and the age distribution of this group of former mine workers was approximately the same as the age distribution of the total group of male lung cancer decedents. Then, after excluding these 21 workers from the risk calculations for males, the resulting SMRs do not indicate statistically significant excesses of lung cancer (ATSDR, 2002a, Tables 7 and 8).

6. Medical testing and Screening Study

In July 2000, ATSDR initiated a medical testing program for Libby residents. Testing was conducted from July to November 2000, and again during the summer of 2001. Participation was voluntary. Subjects either were recruited directly by ATSDR or responded to media advertising. The medical tests included a three-view chest radiograph—posterior–anterior (P–A), right anterior oblique, and left anterior oblique—and a spirometry test. Subjects eligible for testing included former WRG mine workers, and people who had lived, worked, or played in Libby for at least 6 months prior to December 31, 1990. The principal goal of the testing program was to identify asbestos-associated health effects of subjects exposed to asbestos from the mine and, where indicated by the test results, refer them for further medical evaluation. Each subject's test results were evaluated by an on-site radiologist, who determined if a follow-up evaluation was warranted.

ATSDR combined the testing program with a statistical analysis, referred to as a Screening Study, to investigate relationships between radiographic abnormalities and exposure to LA from the mine. Each X-ray film was interpreted by two or three radiologists certified as B-readers,[7] who focused on identifying pleural and interstitial abnormalities. ATSDR classified a subject as a pleural "case" if pleural abnormalities were identified by at least two B-readers using a combination of the oblique and P–A views. An interstitial "case" required at least two B-readers to identify an interstitial abnormality using the P–A view. In addition, ATSDR conducted in-person interviews to obtain demographic and health-related information including age, sex, weight, height, residential history, occupational history, recreational activities and other potential vermiculite-LA exposure pathways, smoking status, medical history (e.g., chest injury or surgery), and self-reported symptoms and illnesses.

[7] Every film was evaluated by at least two B-readers. A third B-reader was employed only if the first two B-readers disagreed on the presence of a pleural abnormality.

In August 2001, ATSDR released a report about the Screening Study that covered results for the first round of testing (6149 subjects). The report described various statistical analyses relating pleural abnormalities to asbestos exposure pathways and potential confounders. ATSDR has not updated its statistical analysis to include results for the 1158 additional subjects during the summer of 2001. Instead, the Agency issued a brief summary of results in September 2002 that covered all subjects who had recent X-rays (ATSDR, 2002b). ATSDR's results included:

- 1186 of the 6668 subjects with chest X-rays (17.8%) had pleural abnormalities.
- The prevalence of pleural abnormalities was highest in WR Grace workers (51%).
- Most subjects reported multiple routes of exposure (household contact, occupational, recreational, and other) and the prevalence of pleural abnormalities increased with the number of exposure pathways.
- 6.7% of the subjects who reported no asbestos exposure pathways had pleural abnormalities.
- Factors associated with higher rates of pleural abnormalities identified through statistical modeling and analysis included: being a WR Grace worker; having household contact with a WR Grace worker; military asbestos exposure; increasing age; being male; smoking; duration of residence in Libby; played in vermiculite piles; higher Body Mass Index.

ATSDR determined the percentage of pleural abnormalities among medical testing participants, 17.8%, and the percentage of participants with pleural abnormalities who claimed no identifiable exposure to asbestos, 6.7%. ASTDR also reported a range of background pleural abnormality rates from other regions of the U.S., 0.02–2.3%. Although not explicitly stated, ATSDR tacitly implied through the juxtaposition of these rates that residence in Libby was a significant risk factor for asbestos-associated pleural disease.

ATSDR's implied conclusion is questionable for two reasons. First, the majority of pleural cases are former mine workers or others who, due to their special activities, were likely to have experienced high level exposures to asbestos. These subjects make up a significant fraction of the 17.8% cases reported by ATSDR, but they are not typical of the majority of residents of Libby. Second, another fraction of the 17.8% may have been identified as cases due to errors in interpreting X-ray films. The potential for misreading pleural fat as a pleural abnormality on X-rays is well documented (Sargent et al., 1984; Proto, 1992; ATSDR, 2003a). Errors of this type may be a contributing factor to the relatively high rate of pleural abnormalities reported for subjects in the Screening Study. In addition, defects in the study design, including the absence of control films and the fact that readers were aware that every film belonged to a subject who had lived in Libby, lead to other potential biases that favor positive diagnoses even where radiographic evidence may not be conclusive. Using a data file prepared by ATSDR that contained the screening data, we investigated: (1) the correlation between LA exposure levels and employment at the mine and (2) factors that play a role in misdiagnosis of pleural abnormalities.

6.1. Asbestos exposure levels

Frequencies and percentages of pleural abnormality diagnoses were compiled for three exposure groups:

Group 1. Participants who were employed by WRG at the Libby mine;

Group 2. Participants who were not employed at the Libby mine, but either had other occupational exposures or domestic exposures[8]; and

Group 3. Participants who had neither occupational nor domestic exposures (also referred to as environmental exposures).

The results are shown in Table 3. Group 1 had the largest percent of pleural cases (51.0%), followed by Group 2 (19.9%), and Group 3 (9.1%). Overall, of the 1186 pleural abnormality cases reported by ATSDR, 971 (81.9%) were in the first two exposure groups—mine workers and other occupationally and domestically exposed participants. These results indicate a correlation between the prevalence of pleural abnormalities and asbestos exposure. Former mine workers, Group 1, would have experienced occupational exposures that were substantially higher than exposures in the other groups. The exposure levels for Group 2, other occupational exposure and domestic exposure, would be expected to be lower as a group average than mine workers' exposures. Group 3 exposures would have been much lower than Group 1 or Group 2 exposures.

These data not only indicate a correlation between pleural abnormalities and asbestos exposure, but also suggest that the prevalence of pleural abnormalities associated with low-level environmental exposures (Group 3) is near the internal background rate, 6.7%, for the Screening Study. These findings, however, may be strengthened or weakened depending on the rate of false positive diagnoses, which may be substantial. The following sections describe analyses of the data that address the false positive issue.

6.2. Adipose tissue and detection of pleural abnormalities

6.2.1. The "FAT?" box on B-reader forms

As a partial solution to misreading sub-pleural fat as pleural thickening or a pleural plaque, the B-reader forms used in the Screening Study included a section for commenting on pleural fat. This section contains a box labeled "FAT?" that provides B-readers with an opportunity to

[8] Domestic exposure occurred where a participant, such as a spouse, shared living quarters with a mine worker and cared for his work clothes.

Table 3
Radiographic identification of pleural abnormalities for three exposure groups in the ATSDR Screening Study in Libby, Montana

	Pleura diagnosis				Total
	Abnormal		Normal		
	Number	Percent (%)	Number	Percent (%)	
Group 1: employed by WRG at the Libby Mine	186	51.0	179	49.0	365
Group 2: other occupational or domestic exposure[a]	785	19.9	3151	80.1	3936
Group 3: no occupational or domestic exposure	215	9.1	2152	90.9	2367
Total	1186	17.8	5482	82.2	6668

[a] "Other Occupational" means occupational exposure, but not at the Libby mine. "Domestic Exposure" means exposure of a spouse or other household contact of an individual with occupational exposure.

Table 4
B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana—all readers

"FAT?" box checked	B-reader forms that identify pleural abnormalities	
	Number	Percent (%)
Yes	893	36.2
No	1574	63.8
Total	2467	100.0

Note. The final category on the B-reader form was labeled "FAT?". A check mark in this box indicated the reader's concern that the abnormalities identified on the form also may be explained by pleural fat.

record their concerns that the observed abnormalities may be explained alternatively as adipose tissue.

Tables 4 and 5 contain a summary of the "FAT?" box results. Table 4 displays results for all B-reader evaluations that indicated a pleural abnormality. Although agreement between two readers led to 1186 pleural cases, a total of 2467 B-reader evaluations identified pleural abnormalities. Of these 2467 evaluations, 893 (36.2%) included a check in the "FAT?" box. Limiting this analysis to the 1186 cases, the "FAT?" box was checked by at least one of the B-readers for 399 subjects, or 28.6% (Table 5). These results suggest that the false positive rate for pleural abnormalities in the Screening Study population may be near 30%.

Table 6 shows that the correlation between sub-pleural fat and a positive diagnosis for pleural abnormalities exists in each of the three exposure groups defined earlier. The data show that the percentage of cases with "FAT?" checked is lowest for mine workers (18.3%) compared to slightly greater than 30% for the other exposure groups. This differential is expected because the mine workers would have had the highest asbestos exposures and, therefore, would have experienced a higher percentage of pleural abnormalities that should not have been confused with sub-pleural fat.

Table 5
B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana—cases

"FAT?" box checked	Pleural abnormality cases	
	Number	Percent (%)
Yes (by at least one B-reader)	339	13.7
No	847	34.3
Total	1186	48.1

See note to Table 4.

6.2.2. Correlation between Body Mass Index and pleural abnormalities

A further assessment of the potential for pleural fat as a source of false positive diagnoses involved investigating the relationship between Body Mass Index (BMI)[9] and the diagnosis of pleural abnormalities for the three exposure groups introduced above.

For each exposure group, Table 7 displays the number and percent of positive and negative diagnoses by BMI category—obese, overweight, normal, and underweight.[10] For Group 1, WRG mine workers, there is no correlation between BMI and the diagnosis. The percentages of subjects in each BMI category are statistically the same for those diagnosed with pleural abnormalities as those diagnosed as normal (p-value = 0.86).

For Group 2, which consists of subjects with other occupational and domestic exposure, BMI is correlated with the diagnosis outcome (p-value < 0.001). A larger percentage of BMI-obese subjects have positive diagnoses in comparison to negative diagnoses (48.5% versus 30.2%) and a smaller percentage of BMI-normal subjects have positive diagnoses in comparison to negative diagnoses (13.8% versus 29.3%).

For Group 3, which consists of subjects with no occupational and no domestic exposure, BMI also is correlated with diagnosis (p-value < 0.001). The pattern of percentages for the BMI categories is similar to the pattern for Group 2: 51.2% of BMI-obese subjects have positive diagnoses versus 30.8% with negative diagnoses; 18.1% of BMI-normal subjects have positive diagnoses versus 33.5% with negative diagnoses.

The results in Table 7 suggest that body mass, absent high level exposures to asbestos, influences positive pleural

[9] Calculated values of BMI were not included in the electronic database received from ATSDR. The height and weight data recorded for each participant was used to calculate BMI. According to the Centers for Disease Control and Prevention, BMI = (weight in kilograms)/(height in meters)^2.

[10] The BMI categories are defined as follows: obese—BMI greater than 30; overweight—BMI between 25 and 30; normal—BMI between 18.5 and 25; underweight—BMI less than 18.5 (CDC).

Table 6
B-reader "Fat?" breakdown for the ATSDR Screening Study in Libby, Montana by exposure group—pleural abnormality cases

"FAT?" box checked		Exposure group 1	2	3	Total
Yes (by at least one B-reader)	Count	34	236	69	339
	Percent	18.3%	30.1%	32.1%	28.6%
No	Count	152	549	146	847
	Percent	81.7%	69.9%	67.9%	71.4%
Total		186	785	215	1186

Notes. Exposure Group 1—WRG mine workers.
Exposure Group 2—other occupational exposure or domestic exposure (i.e., living in the household of an occupationally exposed subject).
Exposure Group 3—environmental exposure (i.e., no occupational or domestic exposure).

Table 7
Correlation between radiographic identification of pleural abnormalities and body mass in the ATSDR medical testing program for Libby, Montana

BMI	Pleural abnormality Number	Pleural abnormality Percent (%)	Pleura normal Number	Pleura normal Percent (%)
Group 1: worked at WRG = 365				
Obese	76	40.9	66	36.9
Overweight	74	39.8	72	40.2
Normal	34	18.3	38	21.2
Underweight	0	0.0	0	0.0
BMI N/A	2	1.1	3	1.7
Total	186	100.0	179	100.0
Test result: no correlation between BMI and identification of pleural abnormality				
Chi square 0.8				
p-value 0.86				
Group 2: other occupational or domestic exposure = 3936				
Obese	381	48.5	951	30.2
Overweight	281	35.8	1238	39.3
Normal	108	13.8	923	29.3
Underweight	7	0.9	23	0.7
BMI N/A	8	1.0	16	0.5
Total	785	100.0	3151	100.0
Test result: statistically significant correlation between BMI and identification of pleural abnormality				
Chi square 123.0				
p-value < 0.001				
Group 3: no occupational or domestic exposure = 2367				
Obese	110	51.2	663	30.8
Overweight	60	27.9	726	33.7
Normal	39	18.1	720	33.5
Underweight	1	0.5	32	1.5
BMI N/A	5	2.3	11	0.5
Total	215	100.0	2152	100.0
Test result: statistically significant correlation between BMI and identification of pleural abnormality				
Chi square 43.1				
p-value < 0.001				

abnormality diagnoses. For mine workers, there is no difference in the distribution of BMI between those diagnosed with pleural abnormalities and those diagnosed as normal. This result is consistent with the hypothesis that pleural abnormalities in mine workers are principally a consequence of high asbestos exposure levels. However, in the two other exposure groups, where asbestos exposure was likely to have been much lower, the group diagnosed as positive has a higher percentage of obesity than the group diagnosed as normal. These data suggest that higher Body Mass Index influences the pleural abnormality diagnoses in a way that could engender false positives.

Table 8
Estimated cumulative lifetime exposure and IRIS risk estimates for Libby residents

Description		PCM			PCME		
		Average level (f/cc)	Estimated lifetime cumulative exposure (f-yr/cc)	EPA IRIS risk	Average level (f/cc)	Estimated lifetime cumulative exposure (f-yr/cc)	EPA IRIS risk
Scenario 1							
Routine activity	Ave	0.0040	0.1023	3.4×10^{-04}	0.0001	0.0026	8.4×10^{-06}
Resident	Max	0.0140	0.3580	1.2×10^{-03}	0.0010	0.0256	8.4×10^{-05}
Scenario 2							
Routine cleaning	Ave	0.0900	0.0411	1.4×10^{-04}	0.0050	0.0023	7.5×10^{-06}
Resident	Max	1.0170	0.4644	1.5×10^{-03}	0.0930	0.0425	1.4×10^{-04}
Scenario 3							
Remodeling	Ave	0.4543	0.0249	8.2×10^{-05}	0.2380	0.0130	4.3×10^{-05}
Resident	Max	1.6200	0.0888	2.9×10^{-04}	0.7040	0.0386	1.3×10^{-04}
Contractor	Ave	0.4543	0.2489	8.2×10^{-04}	0.2380	0.1304	4.3×10^{-04}
	Max	1.6200	0.8877	2.9×10^{-03}	0.7040	0.3858	1.3×10^{-03}
Scenario 4							
Rototilling	Ave	0.1136	0.0083	2.7×10^{-05}	0.0332	0.0002	8.0×10^{-06}
Resident	Max	0.2272	0.0166	5.5×10^{-05}	0.0664	0.0049	1.6×10^{-05}

Source: Average level (f/cc) from Weis (2001, 2002).
Estimated cumulative lifetime exposure and EPA IRIS risk calculated by PAI using factors provided in Weis (2001).

7. EPA exposure and risk analysis

In 2002, EPA added the Libby Asbestos Site to the General Superfund Section of the National Priorities List (NPL), which established Libby as a hazardous waste site requiring clean-up (67 FR 65315 October 24, 2002). As part of the support for the NPL listing, EPA conducted an analysis of exposure and risk for Libby residents and concluded that "... asbestos contamination in various types of source materials at residential and commercial areas in and around the community of Libby, Montana" poses "... an imminent and substantial endangerment to public health" (Weis, 2001).

The analysis was based on air samples collected by EPA associated with four types of activities referred to as Scenarios 1–4. The activities were: Scenario 1—routine activities by a resident; Scenario 2—active cleaning by a resident; Scenario 3 (two parts) a—extensive contact with vermiculite by a contractor, and b—limited contact with vermiculite by a resident; Scenario 4—rototilling a home garden by a resident.[11]

Exposure estimates and risk calculations for the scenarios are displayed in Table 8. The design used for collecting the data was not sufficiently detailed to claim that the results are representative of exposures for Libby residents. Therefore, interpretation and projections based on these results are speculative at best. Nevertheless, EPA argued that the results supported a finding of imminent and substantial endangerment to public health. However, basic interpretation of the results, even without concern about how well they represent residents of Libby, does not suggest a public health crisis. Generally, the risks for residents are within the range considered acceptable by EPA's Superfund program (1×10^{-6} to 1×10^{-4}).

Exposure is reported in Table 8 by PCM and PCME analysis. PCM is the measurement method used by OSHA to enforce its permissible exposure limit (PEL) for asbestos (59 FR 40964 August 10, 1994). PCM cannot distinguish non-asbestos structures that are morphologically similar to asbestos structures. Nevertheless, PCM is appropriate for measuring exposure in an occupational setting where the airborne structures are predominantly asbestos. PCME, which differentiates asbestos from non-asbestos structures, is valuable for measuring airborne concentrations in non-occupational settings where the non-asbestos component of airborne fibers may be substantial. The PCME counting protocol has the same dimension criteria for structures as the PCM method, but includes only asbestos structures (see footnote 4 for details).

The risk estimates in Table 8 represent total cancer (i.e., lung cancer plus mesothelioma) in accordance with the EPA's risk assessment methodology presented in IRIS. Risks calculations are displayed for both PCM and PCME exposure estimates. The difference in exposure and risk between the two methods can be substantial. For most of the scenarios, the reduction in exposure and risk for PCME relative to PCM is approximately a factor of 10.

The risk estimates in Table 8 are very likely higher than the true risks because of EPA's conservative approach to risk assessment. EPA does not consider threshold exposure limits and employs straight-line risk extrapolation from high occupational exposures to low environmental exposures. EPA's conservatism is seen by considering the life-

[11] EPA (2001) contains details about the scenarios.

time cumulative exposures estimated for Libby residents (Table 8). The maximum of these exposure estimates, excluding the Scenario 3b Contractor, which should be assessed as an occupational exposure, is 0.0425 f-yr/cc. This exposure is substantially less than the risk doubling exposure estimates for lung cancer in Table 1 (93–173 f-yr/cc), the lifetime occupational exposure allowed by OSHA's PEL (4.0–4.5 f-yr/cc),[12] and an estimate of lifetime background exposure of 0.40 f-yr/cc. Based on these comparisons, the health risks associated with Libby resident exposure to LA are negligible.

8. Conclusions

Reports prepared by EPA and ATSDR imply, and the news media asserts, that the typical Libby resident is at substantial risk for asbestos-associated disease due to exposure to LA. Upon closer inspection, however, the excess risk projections apply to Libby mine workers who experienced historical high level occupational exposures when the mine was operating. Estimated lifetime cumulative exposures for Libby residents who were not mine workers based on recent air sampling conducted by EPA are low. There is no evidence that LA is more potent for asbestos-associated disease than other types of asbestos. The studies conducted at Libby have not produced sufficient evidence to support the claim that environmental exposures to LA independent of occupational exposures of miners are associated with increased pleural or parenchymal abnormalities, lung cancer, or mesothelioma.

Conflict of Interest

The author has consulted with and conducted studies for W.R. Grace & Co. on various issues concerning asbestos exposure and health risk, including exposure at Libby, Montana. Also, at the request of W.R. Grace & Co., the author has testified in court as a paid export about results of my studies on asbestos exposure and health risk.

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[12] The PEL limits exposure to 0.1 f/cc as a time-weighted average over 8 h. For a 40- or 45-year working lifetime, the lifetime cumulative exposure would be between $4.0(=0.10 \times 40)$ and $4.5(=0.10 \times 45)$ f-yr/cc.

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