Dr. Morris Greenberg
TO DR. Steven Foster

Comment on draft EPA Report:

"Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos."

Declaration of interest

I have provided feed and pro bono opinions on asbestos matters, but have not been funded to produce this comment, nor do I expect to derive any benefit.

Motive for commenting on the EPA draft

I have been involved, over the past forty years, initially in industry and subsequently in the civil service, in the investigation of the adverse health effects of exposure to dusts containing asbestos, and in their amelioration. In connection with this I have also participated in a number of EU/WHO/ILO/IPCS/IARC/EC deliberations. Since retiring I continue to be involved with these organizations, and with pump priming by The Joseph Rowntree Charitable Trust have conducted a programme of historical research on asbestos.

As a consequence, my attention was drawn to this draft document. I am not an American national and can claim no *locus standi* in your councils: my concern is that American practice is advanced to justify unsafe practices in the Third World, particularly effectively in the case of asbestos.

General observations on the EPA draft

Although produced by contractors and disowned by EPA, for convenience, the draft document under discussion will be referred to as EPA's.

It has previously been claimed that the data relating to occupational exposures to asbestos are the best Occupational Health (OH) to be found for any agent. Yet they have been derived from estimates of exposures made during unstructured sampling, variously "personal" or "background". The sampling devices have had significantly varied size selective characteristics, sample durations and volumes have varied widely and exposures have been quantified in terms of weight, or total numbers of particles or fibres of specified dimension ranges per unit volume (Metric or Imperial)

The use of disparate, incomplete and imperfect data to derive a safe exposure standard , has been justified on the need to inform factory managers on "safe" working conditions. In practice, standards have been set with an eye to what is deemed technically and economically achievable in practice.

In common with other agents, with improvement in engineering, to enhance containment, "safe" standards have been lowered. ("This time we really have got it right.")

This EPA draft relies on sophisticated statistical treatments to remedy the deficiencies of the OH data for the derivation of a safe Public Health safety standard. When "acceptable exposure" requires that the excess incidence of specific disease or mortality shall be less than 1:100,000, it must be accepted that for common diseases epidemiological methodology will be unable to provide confirmation with an acceptable degree of confidence.

In deferring the integration of biological data into its deliberations on public health policy to a later date, EPA is in danger of conveying the impression that the mathematical model takes precedence over biological plausibility.

Each page of the draft bears a footnote in 9 point, declaring that the document does not represent an agency determination or policy. Even when typographically enhanced, repeated dire health messages and careful caveats make no impact.

Some problems inherent in the available historic data

In the opinion of the reviewer, the EPA draft is insufficiently informative of how it comes about that exposure data are so poor.

The history of asbestos safety standards from Merewether and Price (1930) onwards is noteworthy for the underlying deficiencies and uncertainties being repeatedly ignored.

The purpose of the EPA document is stated as "*...improvement in the current method that EPA employs for estimating cancer risk from inhalation exposure to asbestos at Superfund sites.*" Attempts to derive a dose response relationship between inhaled asbestos and respiratory malignancy have required to be based on a gallimaufrey of historic exposure data, and on end point data of varying quality.

Problems arising from historic and latterday measurements of environmental contamination by asbestos fibre.

The problems presented in handling historic asbestos exposure data may be considered under four main headings:

[1] Variations in sampling strategy;

[2] Characteristics of sampling apparatus

[3] Measurement criteria;

[4] Reconciling reported data.

Variations in sampling strategy

Sampler sites

Air sampling is conducted to determine dust levels at critical points in an installation (point emission sampling), to provide an indication of general air quality in a workplace (fixed point background sampling), or to measure dust in air presenting at or near the operator nose level (personal sampling).

These samples may be taken over a short period ("snap samples") or over a whole shift and presented as time-weighted averages.

Unless taken by an experienced hygienist, the snap sample may not be representative of the conditions that prevail overall, and time-weighted averaging will not discriminate between a consistent level of exposure and one in which there are unacceptably high peak levels.

Point emission samples serve to determine how effective containment has been and to identify where it may have failed. Background sampling has the merit that the sampler can be positioned where it is least obstructive, but is unsatisfactory as a measure of exposure. Although measuring dust at operator nose level is intuitively appropriate, this has not always seemed so to some hygienists. It has commonly been observed that personal sample readings are higher than background samples.

Sampling Programmes

Even when personal sampling, was employed, because fibre counting is resource and labour intensive, the frequency of testing may have been based on logistic rather than on scientifc grounds. The climatology of an open shop floor may be far from homogenous in all seasons, and processes may change over time. Other practical considerations included whether an individual might act as surrogate for all workers similarly employed.

Historic data collected in structured and unstructured patterns present severe problems of reconciling the various reported studies.

Characteristics of the sampler

The sampler head

Historically, the sampling head was designed and positioned to stop it becoming clogged by large particles, Later it was refined to mimic the selectivity of the human respiratory apparatus.

For the pneumoconioses, sampler head design concentrated on capturing so called "*respirable particles*", defined as those with a high probability of penetrating the airways. Intuitively, such particles penetrating to the lung parenchyma were the cause of silicosis. However, for non-malignant and malignant disease of the airways, the relevant fraction of the inhaled dust that required to be measured was that with a high probability of falling out in the airways.

The sampler

A variety of means have been adopted to obtain total and fractionated samples over the years, adding yet another problem in correlating historic data and even contemporary measurements.

Counting protocol and Quality Control

It took some time for a particle/fibre counting standard to be devised and generally adopted. It required the use of a grid and a protocol for including particles at its margins.

The resource consuming nature of fibre counting, limited enthusiasm for repeated checks of intra- and inter-observer variation. Quality control came late on the scene, but where readers counts for a standard specimen were at the extremes, sanction of laboratories was not common nor were data commonly discarded.

The derivation of standards

The British Standard 1931

The Asbestos Regulations 1931 ostensibly safeguarded the health of workers utterly by not allowing any release of asbestos into the workroom. Existing technology was incapable of containing dust adequately, and there was no respiratory protective equipment that the Factory Inspectorate could approve as efficient in the event of an escape. Despite this it was thought that to prevent the full development of asbestosis amongst asbestos workers within the space of an average working lifetime, it would only be necessary to reduce the concentration of dust in the air of the workrooms to a figure below that pertaining to spinning, designated "the dust datum" A representative air sample of dust arising during flyer spinning obtained during their survey, contained 24 milligrammes of dust per 10 cubic metres of air.

A number of attempts have been made to estimate measures of environmental pollution associated with various processes over time. One such attempt estimated for Ring Spinning:

1930-1965. General Area = 8.2 f/cc, Machine Operator = 6.6 f.cc:

1966-1970, General Area = 8.6 f/cc, Machine Operator = 6.9 f/cc:

1971-1975, General Area= 6.2 f/cc, Machine Operator 5.0 f/cc.

Another set of estimates of dust exposures of men for the years, 1936-1972 was based on a variety of measurements and on 'guestimates' where no measurements had been made. Mean dust levels were estimated to have been: 1936 = 13.3 f/cm^2; 1941 = 14.5 f/cm^2; 1946 = 13.2 f/cm^2; 1951 = 10.8 f/cm^2

Although no attempt had been made to collect data systematically to validate the standard, as late as 1956 a contributor to a textbook on Industrial Health edited by Merewether could assert:

> " ... for all practical purposes the conditions arising from Flyer Spinning carried on without exhaust under good conditions may.be taken as the 'dust quantum'... Nothing has emerged to suggest departure from this practical standard (Meiklejohn, 1956)."

Dreesen

Despite the acknowledged defects of their North Carolina textile factory health data, and inadequate exposure data, Dreesen et al (1938) proclaimed in their abstract:

> "...if asbestos concentrations in the air breathed are kept below the limit [5 million particles [per cubic foot] new cases of asbestosis would not appear."

In the body of the text however, they were more cautious:

> "...5 million particles per cubic foot may be regarded tentatively as the threshold value for asbestos dust exposure until better data are available."

Citing this figure was justified by the authors as despite the data being very poor, factory managers needed some guide as to the working conditions they needed to achieve safety. The 5 mmmcf standard was widely adopted for a variety of other situations and some 40 years were to elapse before an attempt was made in America to evaluate this standard, during which time it was manifestly seriously wanting.

British Occupational Hygiene Society (BOHS)

BOHS concluded that after 50 years exposure to an average atmosphere of 2 fibres per millilitre of chrysotile over 40 hour working weeks, fewer than 2 per cent of workers would have developed early minor signs of lung disease. Because of the limitations of the health and environmental data, of which the analyst was aware, and of other matters that were not taken into consideration, as well as the inability to factor in bronchial carcinoma and malignant mesothelioma, a more conservative figure, well below the lower confidence limit calculated should have been considered. In the event, industry employees on the committee were instructed by the asbestos Trade Association to stand out for the 2 fibre standard.

On reviewing the BOHS 1968 standard, Berry identified its serious defects to include:

[1] That it related solely current employees only (i.e. the sick and the dead were discounted);

[2] That they took no account of the progression that might occur in the future even if there was no future exposure (it had long been appreciated as a feature of asbestosis, that after cessation of exposure, disease often developed);

[3] dust measurements were not available for the early years of exposure and 'guessed' lower limits had been used;

[4] the measurement of health effects was dependent on a single observer (such techniques that were available at the time for reducing observer bias and standardising the reporting of qualitative and quantitative effects had not been employed).

Whereas in his calulation of the BOHS 1968 asbestos standard Berry had concluded that there was a 1%risk of crepitations at a dose of 112 fibers/cm ^{3} years with a 90% lower confidence limit of 51 fibers/cm ^{3} years, in his reanalysis he concluded that there would be a crepitations risk of 9.7%at 112 fibers/cm ^{3} years, and a 1%risk at 43 fibers/cm^{3} years. When ''possible'' and ''certified'' asbestosis were the criteria, he calculated 1% risks at 55 and 72 fiber/cc years respectively. These calculations had been based on measuring risk against cumulative unweighted dust concentration, whose appropriateness the Committee began to question. Simple weighting of asbestos dust exposures against residence time, so that earlier doses were deemed to have more effect than recently acquired doses, produced quite different interpretations. Thus 1% crepitations were forecast to occur after 50 years uniform exposure to a concentration of 0.13 fibers/cm ^{3}, as distinct from the 0.74 fibers/cm^{3} with an unweighted cumulative exposure. When a number of other conjectures were made, and allowances made for the ''clearance'' of fiber from the lungs and for the possibility of a need to allow for a lag period for retained asbestos to act in the development of asbestosis, different conclusions were reached. With the extreme assumptions of a 5-year lag period and a half life of 50 years, Berry's calculations indicated that the hygiene standard of 2 fibers needed to be reduced to a fortieth.

Julian Peto of Oxford University calculated that the standard should be of the order of

0.25–0.3 fibers/cc 12–15 fiber years.

Gardner for the HSC Advisory Committee on Asbestos (ACA)

The exposure data available to Martin Gardner, the ACA's statistician was incomplete, had not been collected systematically, had been obtained by different sampling apparatus, variously as background and personal samples, and quantified in a variety of ways. As a consequence, conversion of the asbestos content of dust samples to the benchmark standard of fibres per cubic centimetre/millilitre, was fraught with considerable uncertainty.

He provided best estimates for (personal) dust levels that would produce various levels of excess mortality for lung cancer alone after 50 years' employment. Using data from three studies, where exposures had been exclusively or predominantly to dust containing chrysotile asbestos, and using three conversion factors, less than 2 per cent excess mortality from lung cancer would be expected at levels ranging from : 11f/cc - 2 f/cc for Canadian miners and millers; 5f/cc - 1 f/cc for American production workers; and 0.8 - 4 f/cc for British

The less than 2 per cent excess mortality criterion of acceptability, had been employed for radiation workers under the imperatives of a World War and its succeeding Cold War nuclear weapon production and civilian energy policies. The development of improved process control in the military and civilian sectors of the nuclear industry, permitted exposures to ionising radiation to be progressively lowered by orders. By the time the ACA started its discussions, the old radiation standard of acceptability had been overtaken by The Royal Society proposals that would require excess death from environmental agents to be less than 1 per 100,000. From the ACA's advisers' tables, the requirement for the excess mortality of asbestos workers from lung cancer alone to be less than 1 per 1,000, would require exposures for the three populations to fall below the ranges : 0.5 - 0.1 f/cc (Canadian data); 0.3 - 0.1 f/cc (American data); 0.04 0.2 f/cc (British data). In its final report, the ACA recommended a control limit for chrysotile of 1 fibre/ml, at which its advisers estimated that the excess total mortality (of asbestosis and of lung cancer) might range in the three study populations: 0.4-2.0 per cent (Canadian); 0.8-4 per cent (American); 1.0-5.0 per cent (British).

The decision to adopt a provisional standard of 1fiber/ml was arrived at after the Committee had deliberated on such health and hygiene data as were available, and after receiving 34 written submissions from industrial users of asbestos, trade unions, other interested organisations, experts and laymen.t

Between 1949 and 1966, dust exposures were measured in Quebec mines by an engineer, but with the initiation of its study, McGill provided the services of a hygienist. Pre-1949 exposures for workers were estimated. Before 1970, environmental dust sampling in the Quebec mines was carried out at various work sites annually, though apparently not systematically, and dust concentrations were expressed in millions of particles per cubic foot (mppcf).

The "Beaudry" Committee's views

"Beaudry" found the McGill study wanting on a number of counts, including:

- *Its measurement of total airborne dust could not provide a precise measurement of asbestos to which workers were exposed.*
- *Dose–response studies were affected by the absence of dust measurements prior to 1948.*
- *The designation of categories of exposure as broad as 400–800 mppcf.y entailed poor precision.*
- *The only exposure data available were derived from the midget impinger*

Despite Berry, who provided the statisteal input to the BOHS 1968 standard, having concluded by then that it presented a greater hazard for asbestosis than had previously been calculated, the causally associated malignancies, still being discounted, "Beaudry" opted for the outmoded 2 fibre standard.

The Ontario inquiry's views

When attempting to reconcile the different measures of asbestos exposure, the Ontario inquiry of 1982 acknowledged inconsistencies between published work and oral evidence about the appropriate factor to apply when converting millions of particles per cubic metre (mppcm) or per cubic foot (mppcf) and fibres per millilitre (f/ml).

Having for a number of years rejected asbestos fibre counting as valid, by now the McGill authors considered that 1 mppcf equalled 3.14 f/cc and suggested that it might be used for other results in the chrysotile mining industry.

In evidence to the inquiry, however, the McGill hygienist declared himself to be unhappy with this conclusion and would have restricted this conversion factor strictly to the precise job distribution in the case–control study from which the figure came.

In his oral testimony, the senior McGill researcher Professor McDonald, considered that his group's attempt to convert particle to fiber measurements:

". . . more or less fizzling out.. . . . We've been doing it for a good five or six years, and I think we know how unanswerable the problem is."

Despite earlier disrecommending fiber counting for monitoring worker exposures in America, and having profound doubts as to the reliability of dose conversion, in the final report on their Quebec miner study, McDonald & Liddell felt confident to equate 300 mppcf.y with 1,000 f/mL.y.

Problems arising from the quality of end point data

Dreesen et al using clinical asbestosis as the end point, employed unreliable data from several American textile plants.

BOHS 1968 purported to fail safe by using the end point of persistent post-tussive rales in an otherwise fit person, and chest radiographs of workers at an asbestos factory were interpreted by its medical officer. In subsequent reviews of these data by their new medical officer and by the same statistician who had calculated the 2 fibre standard, the clinical findings and the radiological data were modified.

The McGill research programme covered: the chest radiograph read in a standardized manner after the ILO/UICC protocol; a standardized respiratory symptom questionnaire; lung function measurements; death registrations. Mortality ended up by being the critical end point studied. The results of a study of a subset of the McGill population by Selikoff in the early 1970s showed a mortality pattern that differed. As for the human health response to Canadian chrysotile, no convincing explanation emerged for the more severe effects observed in North Carolina textile workers as compared with Quebec miners and millers.

Conclusions

In brief, historic exposure and end point data do not permit the derivation of a dose/response relationship from which a Public Health safety standard may be set with confidence.

Even if it were possible to assemble over a long period reliable population health data and environmental data, it is unlikely that epidemiological methodology would be able to validate the predictions made by EPA.

The uncertainty problem is not one peculiar to asbestos: it is shared by other carcinogenic agents, chemical and physical. In the absence of adequate scientific evidence, it is left for value judgements as to acceptability to be made by fully informed populations at risk or by their representatives.