Meeting Notes - GCSA meeting on the Classification and Regulation of Chrysotile Asbestos

10:30-12:30, Monday 7th March 2011
Government Office for Science, 1 Victoria Street, London SW1H 0ET

Attendees

- Chair – Sir John Beddington (Government Chief Scientific Adviser)
- Prof Sir Anthony Newman Taylor (Principal of the Faculty of Medicine, Imperial College London)
- A. Darnton (Epidemiology Unit, Health and Safety Executive)
- Prof J. Peto (Cancer Research UK Chair of Epidemiology at the London School of Hygiene & Tropical Medicine and the Institute of Cancer Research)
- Dr T. Ogden (Chief Editor, The Annals of Occupational Hygiene)
- Dr L. Rushton (Reader in Occupational Epidemiology, School of Public Health, Imperial College London)
- Elizabeth Surkovic (GO Science)
- James Dancy (GO Science)
- Hannah Rees (GO Science)

Executive Summary

All invited experts at the meeting agreed that:

- The available scientific evidence base[a] that drives the scientific literature is of varying quality and is limited, particularly in relation to dose and exposure measurement and the potential for concurrent exposure to other forms of asbestos. It is also difficult to find appropriate comparator or control populations for these studies. Considerable uncertainties in the evidence permit a range of interpretations about the extent of the hazard posed by chrysotile asbestos with respect to mesothelioma and lung cancer. Therefore conclusions drawn from analyses of the literature must be seen in this light.

- There is consistent evidence that chrysotile causes lung cancer, though there is less consistent evidence and more uncertainty with regard to causation of mesothelioma, particularly at low levels of exposure. This supports the current international consensus that chrysotile is carcinogenic, and as such is correctly classified as a Class 1 carcinogen

- Evidence suggests that the relative risk of getting lung cancer from chrysotile exposure compared to amphibole forms of asbestos is within one order of magnitude, when compared at the same exposure levels. The

[a] Please find all of the literature consulted in the reference list in Annex A.

relative risk of getting mesothelioma from chrysotile exposure compared to amphibole is within two orders of magnitude, when compared at the same exposure levels.

- Chrysotile readily breaks down in the lung and is therefore less biopersistent than other amphibole forms of asbestos, but there is insufficient current evidence to determine the toxicological action of chrysotile, and whether there is a linear or non-linear dose response relationship between exposure to chrysotile and causation of lung cancer or mesothelioma i.e. if the carcinogenicity of asbestos fibres is linked to biopersistency in the lung or to cumulative exposure over time

- There is evidence that cancer risk reduces as exposure reduces, and many epidemiological studies imply that exposure to chrysotile can occur at higher levels and for more prolonged exposure periods than amphibole forms of asbestos before an increased risk of cancer becomes detectable. However, it is not possible to determine a threshold level below which exposure to 'pure' chrysotile could be deemed 'safe' for human health. The same applies for exposure to chrysotile from cement during removal and disposal activities.

- There is currently evidence to show that mined chrysotile, or products made from chrysotile in previous decades do have some level of contamination with more dangerous forms of amphibole forms of asbestos. However, the level of contamination may vary greatly, and can only be determined by laboratory testing. There does not appear to be any readily available analysis on purity of current commercial supplies of chrysotile.

The following is a summary of the discussions at the meeting;

Evidence base

1. The group discussed the evidence base available with regard to chrysotile carcinogenicity, exposure and risk. It was agreed that there is a plethora of epidemiological papers and literature; however, there are very few studies which look at exposure to single fibre types i.e. pure chrysotile. This is largely because of the potential bias in studies caused by likely contamination of chrysotile with tremolite (and/or other amphibole forms of asbestos) and their effects on risk.

2. The group discussed the various cohort studies that had been undertaken, in particular those on miners in Quebec[16, 32], and textile factory workers in North and South Carolina[16, 24, 32, 33]. The latter study was deemed to be of the highest quality. However, all agreed that all studies had their limitations given dramatic variation and quality in relation to dose and exposure measurement and analysis. The available epidemiological studies cover a range of different industries and there are therefore different types/fibres of chrysotile in each case. Analysis of these studies

is therefore open to large uncertainties and a potential range of interpretations.

3. The group also discussed the meta-analysis on the Quebec, N & S Carolina other cohort studies undertaken by Hodgson & Darnton (2000)[16] and Berman and Crump (2008)[4]. They noted that Hodgson & Darnton's study was a study of 'commercial chrysotile' as mined and processed with varying amounts of contamination with tremolite. Burman and Crump's study tried to adjust the meta-analysis to take account of contamination and produce risk estimates for absolutely pure chrysotile (though this may not be found in practice). It was agreed that while these are the most comprehensive and best quality meta-analyses, there are also uncertainties in their conclusions given the issues with the individual cohort studies outlined above.

4. Given this, the group agreed that the available scientific literature is of varying quality, little of the human epidemiological literature is of high quality particularly in relation to dose and exposure measurement and the potential for concurrent exposure to other forms of asbestos. It is also difficult to find suitable comparator or control populations for these studies. Considerable uncertainties in the evidence permit a range of interpretations about the extent of the hazard posed by chrysotile asbestos with respect to mesothelioma and lung cancer. Therefore conclusions drawn from analyses of the literature must be seen in this light.

Carcinogenicity, toxicity and classification of pure Chrysotile

5. The group agreed that evidence seemed to broadly indicate that chrysotile does cause pleural plaques, but noted that while pleural plaques are a good indicator of asbestos exposure in themselves, they do not indicate an increased risk of, or act as a precursor to lung cancer or mesothelioma.

6. The evidence demonstrates a low risk of mesothelioma from chrysotile exposure, albeit the North Carolina[24] study and a recent study of an Italian mine[34] may support a higher risk. However, studies clearly show an increased risk of lung cancer associated with chrysotile exposure. The South Carolina cohort is exceptional in showing a much higher risk of lung cancer than other chrysotile cohorts, including those also in the textiles industry that also used amphibole forms of asbestos. This study is one of the best quality studies, though still with limitations. This makes it difficult to conclude whether this plant shows higher risk of lung cancer because the study is of good quality, and other studies underestimate risk, or because there is an unidentified factor which makes this plant exceptional. A view was expressed that one reason for the difference could be that exposures in the Mills in South Carolina involved a high proportion of long fibres[35].

7. In considering whether chrysotile asbestos also causes other types of cancer as stated in the latest IARC review[21] (such as laryngeal, gastro-intestinal and ovarian cancer), it was agreed that the strength of evidence

is variable for different cancers but that it was likely that there would be a much lower risk than that for lung cancer and mesothelioma.

8. The group also considered the hypothesis that all cancer linked to chrysotile could in fact be caused solely by amphibole contamination, and concluded that this could not be conclusively ruled out. However, this seemed highly unlikely given animal studies and some indication of dose response in cohort studies (see paragraphs 12-17).

9. Given this, the group noted that it is difficult, from epidemiological studies, to be confident of the relative contribution to an increase in the risk of lung cancer from chrysotile and from the associated amphibole exposure. Considering this, the group agreed that the meta-analyses by Hodgson & Darnton[16] and Berman & Crump[4] suggest that the relative carcinogenic risk of chrysotile to amphibole forms of asbestos is within about two orders of magnitude with respect to mesothelioma, but for lung cancer the difference may be within a single order of magnitude, when compared at the same exposure levels. The Berman & Crump model shows a higher differential for mesothelioma (since it adjusts for contaminants) but a lower differential for lung cancer (since it places more weight on the higher lung cancer risk of the South Carolina cohort). For a chrysotile exposure of 1 fibre/ml.yrs the Berman & Crump model predicts that an additional 10 lung cancers per 100,000 exposed could be caused by chrysotile (in the context of 5400 lung cancers annually that would occur anyway in the male population, based on the average population level risk).

10. It was also noted that there seems to be a marked difference in risk in different industries.

11. In conclusion the group agreed that there is consistent evidence that chrysotile causes lung cancer, though there is less consistent evidence and more uncertainty with regard to causation of mesothelioma, particularly at low levels of exposure. This supports the current international consensus that chrysotile is carcinogenic, and as such is correctly classified as a Class 1 carcinogen

Exposure Levels

12. The group looked at exposure levels and considered whether there is a threshold below which there is no demonstrable or definable level of risk to human health. The group discussed laboratory studies undertaken on animals looking into carcinogenicity, and noted some limitations given the difference between animal and human models, and the high dose rates used in experiments. The group also noted the pathology undertaken in some of the human cohort studies which showed that amphibole forms of asbestos were usually found in the lung samples, thus providing uncertainty with regard to results for ‘pure chrysotile’.

13. All agreed that the available evidence demonstrates that chrysotile asbestos has a lower biopersistency in the lungs than other asbestos

types, with chrysotile being cleared from the lungs within days to approximately a year, whereas amphibole fibres may persist for many years (although chrysotile fibres have in some cases been observed in the human lung many years after exposure took place).

14. Some studies such as those by Bernstein[5-9] postulate that the lower biopersistence of chrysotile fibres means that the carcinogenic risk is limited to the period it is retained in the lungs. Whereas, it was noted that the Rochdale cohort demonstrated a dose effect insofar as there was a small risk of lung cancer for workers exposed to chrysotile for <10 years, but a much greater risk when exposed for >20 years, but the incidence of lung cancer is increased after shorter periods of exposure to amphibole forms of asbestos. Thus implying that exposure to chrysotile can occur at higher levels and for more prolonged exposure periods than amphibole forms of asbestos before an increased risk of cancer becomes detectable.

15. However, there remains large uncertainty over existing data, and therefore there is insufficient data to determine the toxicological action of chrysotile; in particular, if the carcinogenicity of asbestos fibres is linked to biopersistency in the lung or to cumulative exposure over time. For comparison, cigarette smoke is quickly cleared from the lung, but is clearly carcinogenic. So in the absence of conclusive evidence the low biopersistence of chrysotile is not a conclusive argument against its carcinogenicity.

16. The group noted there is very little reliable data on exposure to chrysotile asbestos at low levels given the high and prolonged exposure rates in the cohort studies, and some animal experiments. Therefore the group discussed modelling of dose/response such as in the Hodgson & Darnton[16] meta-analysis. This study suggests that dose response relationship against risk of lung cancer or mesothelioma may be non-linear, such as is seen with some chemicals. However, there was some question as to whether, given the uncertainty in the cohort studies in particular over exposure estimates, any firm conclusion could be drawn from this.

17. The group concluded that there is insufficient current evidence to determine the toxicological action of chrysotile, and whether there is a linear or non-linear dose response relationship to chrysotile and causation of lung cancer or mesothelioma. It is therefore not possible to determine a threshold level at which exposure to chrysotile could be deemed ‘safe’ for human health.

Contamination of Chrysotile

18. The group had already noted that it is difficult to consider the risk of ‘pure chrysotile’ given the potential contamination with amphibole fibres. On further discussion, it was agreed that available evidence indicates that mined chrysotile is likely to vary greatly in purity/contamination levels with other amphibole forms of asbestos, in particular tremolite. It is also known

that commercial chrysotile products sometimes had amphibole forms of asbestos added to it during the production process, such as in cement and textile product manufacture. Analysis of lung samples from cohort studies from known chrysotile mine and textile workers indicate a level of amphibole contamination, although it cannot conclusively be ruled out that contamination was from another source. Laboratory tests of mined chrysotile or its products have also shown varying levels of contamination.

19. With regard to the purity of chrysotile currently being mined, the group did not know of any information demonstrating the extent of amphibole contamination. Information would have to be requested from industry.

20. However, the group concluded that there is evidence to show that mined chrysotile in the past, and products made from it did have some level of contamination with amphibole forms of asbestos. However, the level of contamination may vary greatly, and could only be determined by laboratory testing. It is therefore difficult to draw firm conclusions about commercial purity of chrysotile products within the UK or currently mined chrysotile.

Asbestos Cement

21. There is evidence to suggest that erosion of chrysotile cement from natural environmental forces, such as acid rain, causes very low levels of fibre release. The group agreed that this was likely to be at such an insignificant level that there was no reason to believe that there is any significant risk to human health from chrysotile contained within cement that is not interfered with.

22. The group also agreed that the relative chrysotile concentration and/or amphibole content in cement are not uniform. The only way of determining this is through laboratory testing.

23. It was noted that, at present, disruptive work on and work to dispose of asbestos cement containing chrysotile will normally be exempt from certain requirements under UK legislation for control of work with asbestos (such as the need to hold a licence from HSE). Nevertheless there are still control measures that should be followed in order to minimise exposure. The EU Directive sets a maximum exposure level of 0.1 f/ml (the current control limit). Long term exposures at this level are likely to be associated with a relatively small increase in the risk of lung cancer.

24. There is some evidence about levels of fibre release that could occur during work with asbestos cement products, but the group agreed that there was limited evidence available with regard to levels of exposure actually occurring as a result of asbestos cement removal and disposal activities. There is therefore little or no evidence to determine the health risk to workers. However, there was agreement that the risk from chrysotile asbestos removal and disposal work would be lower than that

seen historically in cohorts studies, such as in textile factories and mining (given the known relatively high exposure levels in these activities).

25. The group commented that the requirements of HSE asbestos regulations are based on the hazard of the material and a risk assessment relating to the specific work that needs to be carried out. The group discussed the rationale: given the agreed hazard of chrysotile (and potential amphibole forms of asbestos contained in cement products), and the unknown levels of fibre release in asbestos cement demolition or an agreed safe exposure level, that exposure is therefore minimised. The 0.1 f/ml (the current control limit) is not intended to set a safe level, but is part of a framework of measures to help ensure that exposures are reduced as low as reasonably practicable in the context of the lack of scientific certainty.

26. The group did not attempt to do a formal risk assessment: this is clearly the remit of the EU/HSE. But the group commented that the relative risk of lung cancer arising from chrysotile cement during removal and disposal activities is likely to be low, when compared to mining or textile production.

Annex A

The following is a reference list of the papers circulated among the attendees prior to the meeting, some of which are referred to in this meeting note. These documents include all of the evidence received from interested parties, thus include both peer reviewed papers, review papers and opinion pieces. The papers were submitted by the following:

Dr Peter Wright (DWP)
Dr T Ogden (Annals of Occupational Hygiene)
Prof J Peto (LSHTM)
Dr Bob Maynard (HPA)
Prof John Bridle (Asbestos Watchdog)
Andy Darnton (HSE)
Marcondes B. de Moraes (Instituto de Pesquisas Tecnológicas, Brazil)

Peer-reviewed Papers

1. Berman D.W., Crump K.S. (2008) *A Meta-Analysis of Asbestos-Related Cancer Risk That Addresses Fiber Size and Mineral Type* Critical Reviews in Toxicology, 38(S1):49–73

2. Bernstein et al (2006) *The health effects of chrysotile: Current perspective based upon recent data* Regulatory Toxicology and Pharmacology 45 (2006) 252–264

3. Bernstein D M et al (2005) *The Biopersistence of Canadian Chrysotile Asbestos Following Inhalation: Final Results through 1 Year after cessation of exposure* Inhalation Toxicology 17:1-14

4. Bernstein et al (2006) *The Toxicological Response of Brazilian Chrysotile Asbestos: A Multidose Subchronic 90-Day Inhalation Toxicology Study with 92-Day Recovery to Assess Cellular and Pathological Response* Inhalation Toxicology, 18:313-332

5. Bernstein et al (2007) *Misconceptions and Misuse of International Agency for Research on Cancer 'Classification of Carcinogenic Substances': The Case of Asbestos* Indoor Built Environ 16;2:94-98

6. Bernstein et al (2010) *The pathological response and fate in the lung and pleura of chrysotile in combination with fine particles compared to amosite asbestos following short-term inhalation exposure: interim results* Inhalation Toxicology 22;11:937-962

7. Burstyn I. (2010) *The ghosts of methods past: exposure assessment versus job-exposure matrix.* Occup Environ Med 68:2-3

8. Collegium Ramazzini (2010) *Asbestos is Still with Us.* Occupational Medicine 60:584-8

9. Hodgson J, Darnton A. (2000) *The Quantitative Risks of Mesothelioma and Lung Cancer in Relation to Asbestos Exposure* Ann. Occup. Hyg. 44; 8:565-601

10. LaDou J et al (2010) *The Case for a Global Ban on Asbestos* Environ Health Perspect 118:897–901

11. Loomis D, Dement J, Wolf S, Richardson D. (2009) *Lung cancer mortality and fibre exposures among North Carolina asbestos textile workers*. Occup Environ Med 66:535-542

12. Rake C et al (2009) *Occupational, domestic and environmental mesothelioma risks in the British population: a case–control study* British Journal of Cancer 100, 1175-1183

13. Ross M., Nolan R. (2003) *History of asbestos discovery and use and asbestos-related disease in context with the occurrence of asbestos within ophiolite complexes* Geological Society of America Special paper 373

14. Strif K, Benbrahim- Tallaa L, Baan R et al (2009) *A review of human carcinogens_part C: metals, arsenic, dusts, and fibres.* Lancet Oncol 10:453-4

Other Contributions and Evidence

15. Review of the Science Underpinning Asbestos Control Legislation 2011

16. Asbestos : Revising the overall summary analysis of cohorts – “Approach 2” WATCH/2008/5 Annex 1

17. Bridle J., Stone S. Casitile, the New Asbestos: Time to clear the air and save £20 billion

18. Conclusion from 6 experts in the field: ‘On the Safety in use of Chrysotile asbestos’

19. Health Canada, Chrysotile Asbestos Consensus Statement and Summary, Chrysotile Asbestos Expert Panel 2007

20. Health and Safety Commission. (2005) Proposals for revised asbestos regulations and an approved code of practice. HSE Books, Sudbury, Suffolk

21. Hoskins J.A. (1999) Chrysotile in the 21st Century

22. Hoskins J.A., Lange J.H. A Survey of the Health problems associated with the Production and Use of High Density Chrysotile Products

23. HSE Assessment of Recently updated information relating to cohorts with Chrysotile Exposure

24. HSL 2007 Investigation of the chrysotile fibres

25. IARC Monograph Working Group Review 2009: A review of human carcinogens—Part C: metals, arsenic, dusts, and fibres.

26. Summary of Prof J.Bridle's views

27. Maynard B. Comments by Dr Bob Maynard (HPA) on the Classification and Regulation of Asbestos

28. Ogden T L Classification and Regulation of Asbestos Comments by Dr TL Ogden, Chief Editor, Annals of Occupational Hygiene, in answer to the questions in Sir John Beddington's letter of 20 January 2011.

29. Peto J Comments by Prof J Peto on the Classification and Regulation of Asbestos

30. Technology Center for Infrastructure Works Brazil, Civil Construction Material Laboratory (2006) Study of Changes that take place on Asbestos Cement Roofing Sheets throughout their useful life, due to Weathering

The following is a reference list of papers noted at the meeting, but not circulated among the attendees prior to the meeting, some of which are referred to in this meeting note.

31. Sebastien P, McDonald JC, McDonald AD, Harley R. (1989) Respiratory cancer in chrysotile textile and mining industries: exposure inferences from lung analysis. B J Ind Med 46:180-187.

32. McDonald AD, Fry JS, McDonald J. (1983) Dust exposure and mortality in an American chrysotile textile plant. B J Ind Med 40:361-367.

33. Pira E, Pelucchi C, Pialatto PG. (2009) Mortality from cancer and other causes in the Balangero cohort of chrysotile miners. Occ Environ Med 66:805-809.

34. Stayner L, Kuempel E, Gilbert S, Hein M, Dement J. (2008) An epidemiological study of the role of chrysotile asbestos fibre dimensions in determining respiratory disease risk in exposed workers, Occup Environ Med 65:613-619