

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

The carcinogenicity of carbon nanotubes – Presentation by Professor Donaldson

Introduction

1. At the 2008 Horizon scanning discussion, members noted that a pilot study had shown carbon nanotubes (CNT) to cause asbestos like (length dependent) pathology in the mesothelium when injected into the abdominal cavity of mice (Poland et al., 2008, Nat Nanotechnol. 3(7):423-8). Members noted that there was considerable debate about the validity of the models used in such studies, the route of exposure and the high doses used. This was considered to be an area that was worth investigating further and Members stated that they were keen to hear a presentation on the subject. Members confirmed that they were still interested in progressing this subject at the 2009 exercise.
2. Professor Ken Donaldson of Edinburgh University, who is a member of the DH Committee on Medical Effects of Air Pollutants (COMEAP), has kindly agreed to give a presentation of his work on CNT at the July meeting. This paper reminds the Committee of its previous review of nanomaterials and provides a brief introduction to the presentation.

Background

3. CNT are rolled up sheets of graphene¹, which may be capped at one or both ends (see Figure 1 below). They are extremely strong materials which have good thermal and electrical conductivity, are insoluble in water and biologically non-degradable. CNT can exist as compact tangles of nanotubes that are essentially, particles, or as longer, straighter 'fibres'. According to Donaldson et al (2010), the hazard from these two different forms is likely to differ. Particle effects would be confined to the lungs as fibrosis and cancer, whilst fibres are known to have the same types of lung effect but also to affect the pleura.
4. The COC considered an overview of nanomaterial toxicology in 2005 (CC/05/5) and subsequently contributed to a joint COT/COM/COC statement on this topic. The statement proposes an approach to initial toxicological studies with nanomaterials which, in brief, entails identifying the physico-chemical properties and structural characteristics; biodistribution studies; a series of *in vitro* hazard identification tests to assess absorption, cellular response, and release of chemicals from cells; and then confirmation of *in vitro* findings using *in vivo* studies.
5. At the time, there was little information on the potential carcinogenicity of CNT but the COC discussed whether, because of their essentially fibrous structure,

¹ Graphene is a one-atom thick planar sheet of carbon atoms densely packed in a honeycomb crystal lattice.

they might have carcinogenic potential analogous to asbestos. It was concluded that more information was needed before any definite conclusions could be reached. Overall, the committees concluded that the topic of nanomaterial toxicology should be subject to regular reviews.

6. A full review of the recent literature on the carcinogenicity of CNT has not been carried out at this stage but can be brought to the Committee in the future, if Members so wish. Attached is a recently published review by Donaldson et al of the hypothesis regarding the role of long fibre retention in the parietal pleura, inflammation and mesothelioma with reference to work on asbestos and carbon nanotubes. A brief overview of Professor Donaldson's work on the potential mesothelial and pleural toxicities of CNT can be found on pp 12-13 of the review.

7. Lay members may find it useful to see the attached glossary of terms which are used in Professor Donaldson's review and which may be used in his presentation.

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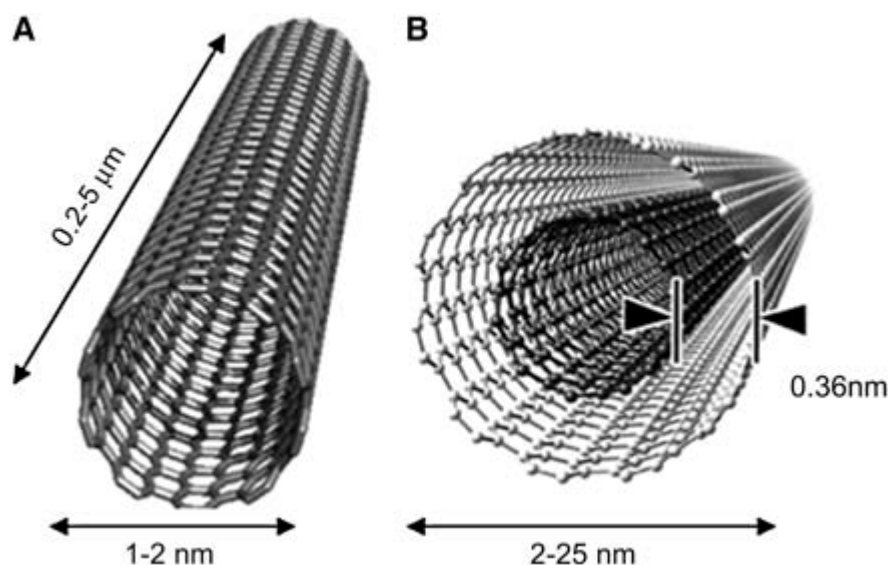


Figure 1: Conceptual diagram of single-walled carbon nanotube (SWCNT) (A) and multiwalled carbon nanotube (MWCNT) (B) delivery systems showing typical dimensions of length, width, and separation distance between graphene layers in MWCNTs.

Glossary of terms

Mesothelium: The layer of cells that lines the *peritoneum* and *pleura*. It is the site of mesothelioma, a tumour most commonly associated with exposure to asbestos.

Parietal pleura: The lungs are surrounded by two thin membranes, the pleura. The outer pleura is attached to the chest wall and is known as the *parietal pleura*; the inner one is attached to the lung and other visceral tissues and is known as the *visceral pleura*. In between the two is a thin space known as the *pleural cavity* or *pleural space*. It is filled with pleural fluid, a fluid produced by the pleura.

Peritoneum: The membrane that lines the walls of the abdominal cavity and folds inward to enclose the abdominal organs.

Phagocytosis: The process whereby certain blood cells (e.g. macrophages) engulf and remove pathogens and solid particles, including fibres. If the blood cell fails to engulf its target, inflammatory chemicals in the cell can be released into the environment (an action referred to as "frustrated phagocytosis"). As these chemicals are also toxic to other tissue, this can lead to extensive damage to healthy cells and tissues.

Pleural cavity/space: see Parietal pleura

Stomata/Stoma: These are narrow (10 micrometres diameter) pore-like tubes which pass through the *parietal pleura* and link the *pleural cavity* with the lymphatic system. They can also be found in the diaphragm where they link the peritoneal cavity with the lymphatic system. Particles/short fibres can drain into the lymphatic system via these stomata.

Visceral pleura: see Parietal pleura