Grouping all carbon nanotubes into a single substance category is scientifically unjustified

To the Editor — The International Chemical Secretariat (ChemSec) recently added carbon nanotubes (CNTs) to the so-called SIN ('Substitute It Now') list of chemicals that they believe should be restricted or banned in the EU[1]. CNTs are the first nanomaterials to be placed on the SIN list. Should this 'designation' concern us as scientists active in the areas of nanotoxicology and nanomedicine? Yes, as it implies that all CNTs can be considered as one material category, which is not the case. Grouping or categorization of chemicals is a valid approach in risk assessment provided that substances with similar properties are grouped together[2]. However, the key (scientific) question is whether all CNTs display the same properties.

Five years ago, the International Agency for Research on Cancer (IARC) classified a particular type of long and rigid CNT, designated as MWCNT-7, as possibly carcinogenic to humans on the basis of available animal studies, whereas all other CNTs were considered 'not classifiable' with regard to their carcinogenicity[3]. The findings of the original evaluation on the inadequate or limited evidence of carcinogenicity for most CNTs were confirmed in a thorough follow-up study a few years later[4]. Hence, while there is no doubt that long and rigid CNTs may cause considerable damage to the lungs following pulmonary exposure (especially when administered at high doses[5]), it is important to note that short and/or tangled CNTs are much less harmful[6,7]. Indeed, it has been demonstrated that the 'asbestos-like' pathogenicity of long CNTs can be alleviated through chemical functionalization, possibly as a result of the effective shortening of the CNTs through debundling or untangling[8]. Chemical functionalization may also impact the stiffness of CNTs, which is perhaps one of the most important parameters with regard to biological reactivity[9].

Most toxicological studies have focused on the length of CNTs owing to the fact that long (>15–20 μm) and biopersistent fibres are known to induce 'frustrated' phagocytosis[4]. However, the diameter and rigidity of CNTs are also important drivers of their biological effects. More specifically, the propensity of CNTs to induce damage to lysosomes — key organelles within the cell — as a function of their biological stiffness has been proposed as a general predictor of the pathogenicity of such materials[10]. Indeed, the rigidity of CNTs is strongly correlated with both acute and chronic inflammation[11]. The take-home message is that not all CNTs are created equal and specific properties including length, diameter and rigidity, as well as the degree of chemical functionalization, determine the biological reactivity or pathogenicity of these materials.

Biopersistence is another important factor that has to be considered. In a study published 10 years ago in this journal, short, single-walled CNTs were shown to be susceptible to degradation by primary human neutrophils[12]. In addition, macrophages have been shown to be capable of digesting multiwalled CNTs[13], and processing of CNTs in microglia — the resident macrophages of the brain — has also been documented[14,15]. Thus, CNTs are not necessarily biopersistent, although the rate of biodegradation may vary depending on the specific material properties. Further studies are needed to address this question.

We concede that the precautionary principle may be a reasonable approach in cases in which data are lacking[1]; however, there are plenty of data to show that CNTs should not be viewed as one material but instead as a class of materials with varying properties that may elicit distinct biological outcomes in vitro and in vivo. □

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