SIN List criticism based on misunderstandings

To the Editor — The addition of carbon nanotubes (CNTs) to the SIN ('Substitute It Now') List by ChemSec[1] made several nanomedicine researchers voice their critique[2,3]. We would hereby like to address some misunderstandings and better clarify our evaluation process as well as the scope and aim of the SIN List.

First, the SIN List is not based on risk assessment, but hazard identification. In the EU, chemical risk assessment is formalized and consists of hazard identification, dose-response assessment, exposure assessment and risk characterization. Hazard identification is related to the assessment of potential sources of harm that a substance has inherent capacity to cause[4]. In the Editorial that accompanied the Correspondences criticizing the inclusion of CNTs in the SIN List[2,3], the terms 'fair' and 'effective' were used in relation to the risk assessment of CNTs[5]. However, the scope and aim of the SIN List is to predict the substances that will or should eventually be added to the Candidate List of Substances of Very High Concern (SVHCs) under the chemical legislation of the EU, known as REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals). Under REACH, these substances would then have to be evaluated for potential authorization or restriction depending on the outcome of a full risk assessment. Adding CNTs to the SIN List — or even to the REACH Candidate List of SVHCs — does not necessarily imply that CNTs will be banned from use in the EU, but it encourages substitution unless safe use can be assured, no alternatives are available or the benefit to society outweigh the risks. The intention of the SIN List is to limit broad and uncontrolled use of very hazardous chemicals. In other words, they should not be used unless risk assessment can prove safe use.

The inherent hazard endpoints used to evaluate whether substances are SVHCs are carcinogenicity, toxicity to reproduction and environmental persistence. The critique raised in the Correspondences mainly focused on the potential carcinogenicity of CNTs and their inclusion in the SIN List as one group of substance; however, it ignored toxicity to reproduction as well as environmental persistence, which were also key factors in our evaluation.

We evaluated evidence for carcinogenicity of single-walled CNTs (SWCNTs), double-walled CNTs (DWCNTs) and multiwalled CNTs (MWCNTs), referring to the review by the International Agency for Research on Cancer (IARC) and we highlighted that the results of genotoxicity studies in vivo and in vitro were positive for both SWCNTs and MWCNTs[1]. We, furthermore, highlighted that lung inflammation, granuloma formation and fibrosis were observed in rats and mice exposed to SWCNTs, DWCNTs or MWCNTs by inhalation, intratracheal instillation or pharyngeal aspiration in the studies reviewed by IARC. As noted by Kuempel et al., both of these findings are significant as genotoxicity and persistent inflammation are considered key events in the development of lung cancer and mesothelioma from exposure to poorly-soluble and fibres, including CNTs[6]. Since the review by the IARC, additional studies on a variety of different types of MWCNTs, for example by Rittinghausen et al.[7] and Sakamoto et al.[8], have been published that support the evidence of MWCNT carcinogenicity after intraperitoneal injection in rats.

Our decision to group all CNTs into one entry on the SIN List is also related to practical reasons, as it is not feasible to address all possible CNT configurations and variations within the scope of the SIN List. We could not by certainty say that some types of CNTs do not share the hazard properties documented for other CNTs. In addition, consumer products containing CNTs are rarely verified to contain only one type of CNT, as purification is costly. It is furthermore a political aim to increasingly address chemicals on a group level under REACH.

The persistency in relevant environmental conditions, which we have discussed in our previous Correspondence on the addition of CNTs to the SIN List[1], is not to be confused with biopersistence, that is, the tendency of a substance to remain inside a biological organism. Indeed, the half-life of carbon nanotubes in the environment is more than 60 days in water and 180 days in sediment and soil, which are the criteria used to designate a very persistent substance under REACH. Biopersistence and degradation of substances in the human body is certainly important with regard to fibre pathogenicity and high aspect ratio nanoparticles[9]; however, this is not what is referred to under REACH or SVHCs criteria for persistency.

Finally, the examples of uses and benefits of innovative applications of CNTs cited by our critics are medical applications. However, the critique towards the proclaimed negative implications of the SIN Listing of CNTs on medical applications and scientific research and development in general is misplaced as these are exempted from REACH. ❐

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