Review of the NIOSH draft *Current Intelligence Bulletin: Occupational Exposure to Carbon Nanotubes and Nanofibers* (November 2010 draft)

March 17, 2011

I have reviewed the November 2010 NIOSH draft *Current Intelligence Bulletin: Occupational Exposure to Carbon Nanotubes and Nanofibers* ("CIB"), as well as the transcript of the February 3, 2011 public meeting and the 26 public comments submitted subsequent to the public meeting which were provided to me in the February 23, 2011 email from Dr. Richard Niemeier. Below are my comments with respect to the specific charge questions submitted for peer review, followed by general comments.

1. Is the hazard identification and discussion of health effects for CNT and CNF a full and reasonable reflection of the animal studies and other scientific evidence in the scientific literature?

The CIB provides a complete review of the available (as of mid-2010) peer-reviewed toxicological health effects data for single and multi-wall carbon nanotubes as well as carbon nanofibers. The interpretation and discussion of the study results, as well as the strengths and weaknesses of the various study methodologies, is appropriate.

2. Is the risk assessment and dosimetric modeling methods used in this document appropriate and relevant?

The risk assessment and dosimetric modeling methods utilized in the CIB represent the current state-of-the-art for this type of application. The authors of the risk assessment have appropriately utilized a benchmark dose (BMD) approach to modeling the toxicological data from the relevant selected studies, and have appropriately noted the limitations of the available data for use in the applied BMD methodology. Primary emphasis should be placed on the risk assessment results calculated from the two sub-chronic inhalation studies (Ma-Hock et al. 2009, Pauluhn 2010) which are most relevant to the human route of exposure and exposure periodicity. The short-term instillation and aspiration studies provide information on potential hazard and mode of action, but are of limited utility for use in extrapolating human health risks.

I concur with the thrust of the public comments on the CIB regarding the need for a sensitivity analysis that discusses which step(s) constitute the greatest source of uncertainty with respect to the multi-step methodology used to develop the risk assessment. Such an uncertainty analysis would provide the reader with a perspective on which of the numerous steps (and associated data selection and assumptions) of the risk assessment methodology are of greatest influence on the

uncertainties associated with the final risk characterization. The uncertainty analysis would also be informative for indicating which aspects of the risk assessment would benefit greatest from investment in further research and data development. While a quantitative sensitivity analysis would be preferable, at a minimum a qualitative assessment of which components of the risk assessment present the largest sources of uncertainty should be included in the CIB.

3. Is the use of respirable mass as a dose metric appropriate for estimating worker risks from inhalation to CNT and CNF?

Since mass-based dose (for the instillation and aspiration studies) or mass-based exposure (for the inhalation studies) was the only available consistent exposure metric reported in the animal studies upon which the estimated human health risks were based, respirable mass is the only currently available basis for extrapolation of the full body of animal study data in estimating worker risks. However, future animal and human studies will hopefully provide information on exposure metrics (e.g., tube or fiber number and size, surface area) that based on experience with other fibers such as asbestos as well as ultrafine particles are likely to prove more relevant to estimating worker risks than a mass-based metric. Therefore, the use of respirable mass as the basis for estimating worker risks should be revisited as part of an expedited review of the scientific literature on CNT/CNF to determine whether an update of the proposed recommended exposure limit (REL) is warranted.

4. Are the sampling and analytical methods adequate to measure worker exposure to carbon nanotubes and nanofibers?

The selection of a monitoring method that measures elemental carbon mass is not likely to provide information on the CNT/CNF exposure metric of greatest relevance to assessing human health risks. The rationale presented in the CIB for selection of NIOSH Method 5040 rests primarily on it being the pragmatic approach to a broad-scale CNT/CNF monitoring protocol due to current cost and technological feasibility considerations. However, I concur with the recommendation made in the comments of the Dutch Expert Committee on Occupational Safety that the CIB strengthen language that encourages the use of additional analytical techniques discussed in the CIB such as TEM for work environments with the highest likely exposure potential. The CIB would benefit from additional discussion of other potential sampling and analytical methods (e.g., TEM) that could be used to augment the NIOSH Method 5040 with regard to measuring worker exposure to CNT/CNF in potentially higher risk work environments. Expanded discussion in the CIB of the characteristics of potentially higher risk work environments would be beneficial to supplement a recommendation for additional monitoring protocols for such work environments.

5. Are there additional relevant studies or methods that NIOSH should consider in developing the REL for CNT and CNF?

As discussed above, the REL for CNT/CNF should include reference to use of a TEM monitoring protocol (e.g., NIOSH Method 7402) for work environments with the highest likely exposure potential.

General Comments

The CIB notes that the proposed REL for CNT and CNF is based on the limit of quantification (LOQ) for the NIOSH Method 5040 rather than on a level of exposure that provides adequate worker protection from excess health risks (CIB pgs. 6-7). Further, the CIB acknowledges that current scientific evidence suggests that use of exposure metrics such as number concentration of defined CNT/CNF dimensions are likely a better predictor of adverse health effects such as lung fibrosis than the use of a mass-based exposure metric, and that NIOSH Method 5040 may not be sufficiently sensitive to fully capture CNT/CNF concentrations at low volume levels (CIB pg. 7). As noted in the review of occupational exposure limits (OELs) for nanomaterials by Schulte et al. (2010), the Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA) and the British Standards Institution (BSI) have proposed occupational exposure limits for carbon nanotubes and fibrous nanomaterials respectively of 0.01 f/cm^3. An assessment of the strengths and weaknesses of the IFA and BSI recommended OELs, and NIOSH's rationale for not adopting an REL consistent with that of the IFA/BSI OELs, would provide the reader with a useful comparison to the 7μg/m^3 REL proposal.

The comments above should not be construed as opposing the adoption of the proposed REL of 7μg/m^3 as an interim recommended exposure limit that should be reviewed and if necessary updated as soon as possible to consider whether an REL based on an alternative exposure assessment approach that is likely to be more reflective of the potential human health risks, e.g., CNT/CNF number and size-based exposure metric, should be adopted. Such an approach would encourage the monitoring technology industry to invest in the development of reasonable cost equipment for such measurement approaches with the understanding that a substantial market will develop for assessments of these metrics.

References

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