

## **Dragon, Karen E. (CDC/NIOSH/EID)**

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**From:** robert.landsiedel@basf.com  
**Sent:** Friday, February 18, 2011 3:07 AM  
**To:** NIOSH Docket Office (CDC); Niemeier, Richard W. (CDC/NIOSH/EID)  
**Cc:** Kuempel, Eileen (CDC/NIOSH/EID)  
**Subject:** Comments/Review: NIOSH CIB CNT  
**Attachments:** NIOSH\_CNT\_CIB\_comments\_BASF\_2011\_02\_15\_.pdf

Dear Madame or Sir,

Please find enclosed our comments on the *NIOSH Current Intelligence Bulletin: Occupational Exposure to Carbon Nanotubes and Nanofibers*. Our comments are arranged according to the five questions :

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?
2. Is the risk assessment and dosimetric modeling methods used in this document appropriate and relevant?
3. Is the use of respirable mass as a dose metric appropriate for estimating worker risks from inhalation to CNT and CNF?
4. Are the sampling and analytical methods adequate to measure worker exposure to carbon nanotubes and nanofibers?
5. Are there additional relevant studies or methods that NIOSH should consider in developing the REL for CNT and CNF?

mit freundlichen Grüßen, best regards  
Robert Landsiedel

### **Dr. Robert Landsiedel**

BASF Product Safety - Experimental Toxicology and Ecology

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| Von:     | "Niemeier, Richard W. (CDC/NIOSH/EID)" <rwn1@cdc.gov>                      |
| An:      | robert.landsiedel@basf.com   |
| Datum:   | 08.12.2010 17:49   |
| Betreff: | Stakeholder review of NIOSH CIB on Carbon Nanotubes and Nanofibers (Plain) |

Dear Dr. Landsiedel:

The National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention (NIOSH, CDC) is conducting a review of the NIOSH scientific document entitled *NIOSH Current Intelligence Bulletin: Occupational Exposure to Carbon Nanotubes and Nanofibers* (attached). This document has been determined by NIOSH to be a Highly Influential Scientific Assessment according to the Office of Management and Budget (OMB) guidelines under the Federal Data Quality Act 2000 (Public Law 106-554, Section 1(a)(3)[515]). The document summarizes the literature describing the adverse lung effects observed in laboratory animals exposed to carbon nanotubes (CNT) and carbon nanofibers (CNF). The purpose of the CIB is to disseminate recent information about the potential respiratory hazard to workers exposed to CNT and CNF. The intended audience of the CIB is health professionals and regulatory agencies, although the recommended risk management guidance provided in the document can be used by employers and workers where exposures to CNT or CNF occur. This guidance document does not have the force and effect of law. The document is also posted on the NIOSH website at <http://www.cdc.gov/niosh/docket/review/docket161A/default.html>

The goals of the document are to (1) describe the relevant animal and other scientific evidence on the health effects of CNT and CNF, (2) provide a quantitative risk assessment based on dose-response information from the animal studies, (3) describe the rationale NIOSH used in the development of the draft recommended exposure limit (REL), (4) provide recommendations on how to minimize worker exposure, and (5) provide guidance on how to implement an occupational health surveillance program (hazard and medical).

As a stakeholder, we are requesting your participation in the review process. The charge to the reviewers is to objectively review the document to determine whether:

- the hazard identification is a reasonable reflection of the available scientific studies,
- the risk assessment and dosimetric modeling represent a reasonable methodology for estimating worker risks from exposure to carbon nanotubes and nanofibers,
- the data and analysis used by NIOSH are appropriate for the scientific conclusions that formed the basis of the proposed REL, and
- the recommendations (e.g., risk management, occupational health surveillance) for protecting worker's health are reasonable and appropriate

To facilitate review of this Current Intelligence bulletin, the five questions below should be considered:

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?
2. Is the risk assessment and dosimetric modeling methods used in this document appropriate and relevant?
3. Is the use of respirable mass as a dose metric appropriate for estimating worker risks from inhalation to CNT and CNF?
4. Are the sampling and analytical methods adequate to measure worker exposure to carbon nanotubes and nanofibers?
5. Are there additional relevant studies or methods that NIOSH should consider in developing the REL for CNT and CNF?

Please address only the technical content of this document. The document will have an editorial review after revisions are made based on external peer reviewer and stakeholder comments.

A public meeting will be held on **February 3, 2011** at the

Millennium Hotel Cincinnati,

Grand Ballroom A,  
150 West 5th Street,  
Cincinnati, OH. 45202,

9:00 AM-4:00 PM (GMT-05:00) Eastern Standard Time.

This will be a forum for scientists and representatives of government agencies, industry, labor and other stakeholders and to discuss the document. The meeting will be open to the public, limited only by the space available. Your attendance at the meeting is optional; if you plan to attend the meeting please contact Diane Miller by January 28, 2011 at the address given below.

We request that your written review comments be submitted by the close of the public docket on **February 18, 2011**. Please return your written comments either by mail (to Diane Miller, NIOSH Docket Office, Robert A. Taft Laboratories, Mail Stop C-34, 4676 Columbia Parkway, Cincinnati, Ohio 45226) or send electronically via e-mail to [nioshdocket@cdc.gov](mailto:nioshdocket@cdc.gov). All electronic comments should be formatted as Microsoft Word. Please make reference to docket number **NIOSH 161-A** when you submit your comments. Please be aware that your name, affiliation, and comments will be posted on the NIOSH website along with a peer review report containing the peer review comments and the NIOSH response to each comment.

We greatly appreciate your review of this document and look forward to obtaining your input. If you have questions regarding the document that you wish to discuss, please contact Dr. Rick Niemeier at (513) 533-8388 or [rwn1@cdc.gov](mailto:rwn1@cdc.gov). Thank you for your assistance in this important review process.

Sincerely, Rick

Richard W. Niemeier, Ph.D.

Senior Scientist/Toxicologist

Associate Director for Science

Education and Information Division

NIOSH

**Comments on  
NIOSH Current Intelligence Bulletin  
Occupational Exposure to Carbon Nanotubes and Nanofibers**

by

Robert Landsiedel, BASF Experimental Toxicology and Ecology, 67056 Ludwigshafen, Germany  
Karin Wiench, BASF Product Safety, 67056 Ludwigshafen, Germany  
Stefan Engel, BASF Occupational Safety, 67056 Ludwigshafen, Germany

**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?**

NIOSH combined the data from several studies with different CNT and very few with CNF, using different airway exposure techniques.

NIOSH has used all available and relevant toxicological studies and interpreted the individual toxicological data correctly. The extrapolation of rodent data to a human-equivalent dose assumed, however, that responses to lung burdens are equal in rodents and humans. This, however, ignores higher susceptibility of rodents due to overload of their lung clearance.

NIOSH has grouped the data to draw general conclusions on all CNT and CNF materials. Yet, different substances showed – in part - very different effects and therefore do not justify a common assessment.

Likewise, materials in inhalation studies may well cause effects different from effects found by direct administration to the lung (intratracheal instillation and oropharyngeal aspiration).

Remarkably, NIOSH did not differentiate fiber-specific effects and general effects of (glomerular) particles in the lung.

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

NIOSH has used the benchmark dose approach for the risk assessment; this is an appropriate model for these data. With the exception of studies using single dose only.

NIOSH selected an estimate of lung burden rather than airborne concentrations as a dosimetry. By taking this approach it was possible to include the data from studies with direct administration to the lung (intratracheal instillation and oropharyngeal aspiration) along with data from inhalation studies.

Deposited lung burden is, however, calculated based on a model validated for spherical particles and may thus be inaccurate.

Moreover, for carbonaceous material, the lung burden is not measured but merely calculated from the airborne concentrations. Therefore it is a data transformation through an unvalidated model which may add to the uncertainty of the dosimetry.

Furthermore, the dosimetry does not adequately consider size distributions, heavy metal (catalyst) contents and, agglomeration states of the administered material.

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

NIOSH uses mass as a dose metric, which is a pragmatic approach. Basically, mass concentration can be converted into other metrics such as total fiber number concentration or total surface area concentration. An accurate conversion can, however, not be accomplished as assumptions have to be made for the length and diameter of a reference fibre and any information on the fibre size distribution is not possible.

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

NIOSH refers to the measurement method (5040), which was developed to measure diesel particulate matter as elemental carbon. The method is not validated for CNT or CNF. The method is disturbed by any confounding emission source releasing carbonaceous material. The distinction from the aerosol background concentration is thus cumbersome and not possible without additional sampling followed by subsequent, appropriate off-line analysis, as for example electron microscopy. However, morphological information is required to provide evidence of CNT release rather than exposure to the aerosol background.

It is recommended to consider to (additionally) assess CNT by their catalyst content using metal or metal oxide residues as a tracer. This may be more specific and may also yield lower LOQs.

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

NIOSH based its CIB on the LOQ of the best-available analytical methods. Calculated lung burdens were used to derive human equivalent doses.

Both approaches are somewhat imperfect. Instead, no-observed-effect concentrations from inhalation studies present an alternative directly utilizing airborne concentrations and biological effects.