FINAL

PEER REVIEW SUMMARY REPORT

External Peer Review of EPA's Letter Peer Review Draft Report
Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

Prepared for:
Christina Powers, Ph.D.
U.S. Environmental Protection Agency
National Center for Environmental Assessment
109 T.W. Alexander Drive (B243-01)
Research Triangle Park, NC 27709

Prepared by:
Versar, Inc.
6850 Versar Center
Springfield, VA 22151

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Peer Reviewers:

Karin Aschberger, Ph.D.
Jaclyn Cañas-Carrell, Ph.D.
P. Lee Ferguson, Ph.D.
Fadri Gottschalk, Ph.D.
Stig I. Olsen, Ph.D.

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I. INTRODUCTION

The Environmental Protection Agency (EPA) *Nanotechnology White Paper*[1], under the heading of Risk Assessment (Section 6.2.7 of the White Paper), recommended developing case studies of engineered nanomaterials and conducting workshops to identify data gaps and research needs related to assessment efforts. Subsequently, the EPA's National Center for Environmental Assessment (NCEA) developed the 2012 draft document *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles*[2] (hereafter MWCNT Case Study External Review Draft [ERD report]). The MWCNT Case Study is the third in a series of such documents[3,4] and serves as another step in refining a strategic approach for nanomaterials risk assessment research, consistent with objectives described in the EPA *Nanomaterial Research Strategy*[5].

The case studies were constructed with the comprehensive environmental assessment (CEA) framework, which is a key element of the CEA process to engage expert stakeholders with diverse perspectives in prioritizing information to support research planning or risk management decisions[6,7]. To date, the intent of developing the CEA case studies has been to support research planning by organizing information on nanomaterials in a manner that facilitates thinking about information gaps that, if pursued, could support future assessment and subsequent risk management efforts. As such, the case studies have not been developed as actual or even preliminary assessments, nor are they meant to provide an immediate basis for risk management, regulatory, or policy decisions.

Similar to previous case studies, the MWCNT Case Study ERD was made available for public comment through a Federal Register Notice. Along with receiving public comments, EPA held a Public Information Exchange meeting on October 29, 2012 to provide information on the MWCNT Case Study ERD and receive comments and questions from the public. Following the conclusion of the Public Information Exchange meeting, Research Triangle Institute (RTI) International conducted an EPA-funded workshop in the same location called *Nanomaterial Case Study Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon*

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[1] U.S. Environmental Protection Agency (2007) *Nanotechnology White Paper.* Science Policy Council, Washington, DC. EPA 100/B-07/001, February. Available at: http://www.epa.gov/nanoscience/files/epa_nano_wp_2007.pdf.

[2] U.S. Environmental Protection Agency (2012) *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles* (External Review Draft). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-12/0843A. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=244011.

[3] U.S. Environmental Protection Agency (2012) *Nanomaterial Case Studies: Nanoscale Titanium Dioxide in Water Treatment and Topical Sunscreen* (Final). ORD, NCEA, Washington, DC. EPA/600/R-09/057F, November. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=230972.

[4] U.S. Environmental Protection Agency (2010) *Nanomaterial Case Study: Nanoscale Silver in Disinfectant Spray* (Final). ORD, NCEA, Washington, DC. EPA/600/R-10/081F, August. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=241665.

[5] U.S. Environmental Protection Agency (2009) *Nanomaterial Research Strategy*. Washington, DC. EPA 620/K-09/011, June. Available at: http://www.epa.gov/nanoscience/files/nanotech_research_strategy_final.pdf.

[6] Davis, JM. (2007) How to assess the risks of nanotechnology: learning from past experience. J Nanoscience and Nanotechnology 7: 402-409.

[7] Powers, CM; Dana, G; Gillespie, P; Gwinn, MR; Hendren, CO; Long, TC; Wang, A; Davis JM. (2012). Comprehensive environmental assessment: A meta-assessment approach. Environ Sci Technol 46(17): 9202-9208.

Nanotubes on October 29-31, 2012. The goal in preparing the MWCNT Case Study ERD and holding the workshop was to identify and prioritize research needed to support future assessments and subsequent risk management efforts for MWCNT. Therefore, the current Peer Review Draft (PRD) of the report (March 2013) reflects which areas expert stakeholders at the October 2012 workshop, identified as research priorities (i.e., those that experts identified as "important to consider in future risk assessments of MWCNTs" but for which they generally lack confidence in the current state of the science to support risk management decisions). Each chapter of the PRD report is briefly described below.

- Chapter 1 is an introductory chapter that describes the CEA approach and presents other background information.

- Chapters 2-5 present information on MWCNTs (i.e., the product life cycle, environmental transformation, transport, and fate, exposure, dose and impacts). In addition, information is provided on a conventional flame-retardant material, decabromodiphenyl ether (decaBDE), which is also used in upholstery textiles. The primary purpose of this comparative information is to provide a more robust database as a foundation from which to identify data gaps related to MWCNT flame-retardant coatings applied to upholstery textiles.

- Chapter 6 discusses the rest of the PRD report in the context of linking research planning to future assessments and risk management efforts, explaining how the ERD report supported engaging expert stakeholders with diverse perspectives in a structured collective judgment prioritization of research gaps for MWCNTs, and highlighting research priorities identified through the expert engagement process.

- Appendices present supporting information for the main body of the PRD report, as well as results of a pilot project to present information in the case study using knowledge maps. In addition, one appendix presents a record of comments and response to comments on the MWCNT Case Study ERD. As noted above, information throughout the document focuses on the priority areas that emerged from the *Nanomaterial Case Study Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes*.

The 2012 ERD of EPA's *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles* was revised to create the PRD report, based on comments received from workshop participants and the public. This Peer Review Summary Report reflects the outcomes of NCEA's request for a letter review of this revised 2013 PRD report by individuals with expertise in one or more topic areas related to life cycle and risk assessment of nanomaterials.

Peer Reviewers:

Karin Aschberger, Ph.D.
European Commission - Joint Research Centre
Ispra, Italy

Jaclyn Cañas-Carrell, Ph.D.
Texas Tech University
Lubbock, TX

P. Lee Ferguson, Ph.D.
Duke University
Durham, NC

Fadri Gottschalk, Ph.D.
ETSS / ETH
Zurich, Switzerland

Stig I. Olsen, Ph.D.
Toxicon v/Stig Olsen
DK-2880 Bagsvaerd
Denmark

II. CHARGE TO REVIEWERS

The 2012 ERD of EPA's *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles* was revised for the PRD report, based on comments received from workshop participants and the public. NCEA is requesting a letter review of this PRD report, by individuals with expertise in one or more topic areas related to life cycle and risk assessment of nanomaterials. Charge questions to guide the review are listed below. Following the review, NCEA staff will revise the case study further, to consider comments from the peer reviewers.

Charge Questions:

Completeness and Accuracy

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

Clarity and Use of Priority Areas to Support Research Planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? *Throughout the 2013 PRD report, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the 2012 MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."*

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

Potential Utility of Knowledge Maps

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

III. QUALITY NARRATIVE STATEMENT

This section details the quality assurance procedures that were followed to conduct this external peer review. Versar has a well-established approach to conducting peer reviews, from reviewer selection through completion of the final report. Within this approach are several quality assurance protocols to ensure that: qualified individuals are selected to participate, they are free from conflict of interest (COI) and the appearance of the lack of impartiality, and a thorough review is completed.

Reviewer Identification and Selection

Versar's approach for selecting the technical expert reviewers consisted of the following five key steps: (1) development of selection criteria, (2) identification of experts, (3) COI screening, (4) selection of peer reviewers, and (5) confirmation of peer reviewer participation.

The experts that participated in this review were identified by literature searches of scientific journals, professional societies, and scientific meetings, as well as searches of Versar's internal peer review database of more than 3,000 scientists. As a result of this search, Versar identified a total of 34 potential scientific experts with expertise in the general area of life cycle and risk assessment of nanomaterials. Interested candidates provided their *curriculum vitae*, which was reviewed by two Versar staff members to ensure that each candidate had the appropriate scientific credentials and evidence of expertise through a listing of their publications and professional affiliations. The specific areas of expertise needed for the peer review included: (1) analytical methods for characterizing nanomaterials; (2) life cycle stages for MWCNTs; (3) transport, transformation, and fate of MWCNTs; (4) exposure, dose, and translocation of nanomaterials; (5) ecological effects of MWCNTs; and (6) health effects of MWCNTs.

Versar also conducted COI screening to make certain that the experts had no COI or appearance of the lack of impartiality. This screening involved sending the potential candidates a series of COI screening questions that helped us to determine if they were involved with any other work and/or organizations that might create a real or perceived conflict of interest for the current task. Additionally, each expert signed forms certifying that, to the best of their knowledge, they did not have any conflict of interest related to the task. Upon completion of the COI screening, Versar selected five experts, based on their credentials, to conduct the review. Versar requested consent from the EPA Task Order Project Officer (TOPO) and EPA acknowledged that the proposed candidates were qualified to participate in the review. Subsequently, Versar contacted the five reviewers to notify them that they were selected to participate in the peer review.

Conducting the Review

Following the selection process, Versar distributed to the reviewers EPA's 2013 MWCNT PRD document *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles,* which included public comments and EPA's responses on the previous 2012 ERD report. Versar also distributed instructions for accessing EPA's Health and Environmental Research Online database (HERO) so that reviewers could easily access the references listed in the PRD report. In addition,

Versar provided to reviewers a work assignment authorization (WAA) letter, which included the charge questions, instructions, and a template for the preparation of written comments to ensure that each reviewer submitted their comments in a consistent format. The WAA also included Versar's confidentiality statement indicating that the peer reviewers' should not distribute or discuss their comments with any outside party, as well as the amount of time the external reviewers had to complete their reviews and submit written comments. During the review period, Versar monitored the progress of the reviewers on a weekly basis in order to make sure there was timely delivery of the written comments.

Review of Expert Comments

At the completion of the review period, Versar evaluated the experts' comments for completeness and scientific quality, organized them into a final peer review summary report, and submitted them to EPA. The five experts all submitted thorough reviews of the PRD report. The experts provided (1) general comments, which included their overall impressions of the document, addressing the accuracy of information presented, clarity of presentation, and soundness of the conclusions; (2) responses to 11 charge questions; and (3) specific observations, which included corrections or changes to the document.

IV. GENERAL IMPRESSIONS

Karin Aschberger

The document provides a comprehensive overview on the use of MWCNTs as flame retardants in textiles. It covers important issues such as life cycle, transport/fate, exposure, and hazard, and gives recommendations for identifying and prioritizing research needs. The document is very clear and interesting to read.

According to the title, a comparison to DecaBDE flame retardant coatings should be made. This relates more to the previous version (July 2012 for public consultation) of the document, where MWCNT was set in direct comparison to Deca BDE. In the current document, most of the content on Deca BDE was moved to an Annex, which is appreciated as the document focuses more on MWCNTs; however, a change in the title could be envisaged to better fit the current scope.

I am not completely sure how much DecaBDE contributes to inform MWCNT assessments in relation to the research priorities, as these are very different compounds with different characteristics and behaviour in the environment and in the human body. In my review, the comparison should relate more to the (expected) risks and MWCNT could be used as an alternative to the phased out DecaBDE. For this, a general overview with comparisons could be presented.

In addition, MWCNT cannot be used alone in textiles (and other applications) as flame retardants because they do not comply with the flammability test and instead are used with other flame retardants to decrease the flammability synergistically. Therefore, in my view, it is not adequate to directly compare MWCNT alone with DecaBDE. A representative compound which is used in combination with CNTs (e.g., phosphonates) should be included in the comparison.

Additional Information:

- Just a remark. 'Comprehensive Environmental Risk Assessment' – as a European, I was wondering about the 'Environmental' as we usually speak about ' Human Health and Environmental' and would not consider Human Health to be included in an Environmental Risk Assessment.

- Our group is currently taking part in the FP7 Project 'DEROCA' *Development of safe and eco-friendly flame retardant materials based on CNT co-additives for commodity polymers.* Our task is a comparative risk assessment to other flame retardant solutions. If you are interested (we have just started and no results yet available), here is the website link: http://www.deroca.eu/DEROCA_WEB/UK/Home.awp

Jaclyn Cañas-Carrell

Overall, the case study document is very well written, organized, and very informative. It is a bit strange that the case study is so focused on one type of application of MWCNTs, especially one that is not the most common application and one that may never become a major application of MWCNTs. However, the majority of the information and Priority Research Areas included in the document provides guidance for general research needs for MWCNTs, independent of the application. Therefore, this document will be of use to CNT and MWCNT researchers even if these nanomaterials are not widely used in flame-retardant textile coatings.

The presentation of the literature and the identified Priority Research Areas was clear and informative to drive future research directions to ultimately support risk assessment and management of MWCNTs.

With regards to presentation of the document, it is well organized and presented in a very logical manner. The introductory chapter does an excellent job at setting the stage for the remainder of the document as well as providing a context for why decaBDE is included in the document. The extensive use of headings and subheadings is very useful to the reader. The use of various text boxes highlighting important information and identifying Priority Research Areas really allowed for the most important information to be clearly stated and stand out to the reader. Overall, the document is easy to read and is presented in a clear and logical manner.

P. Lee Ferguson

My overall impression of this case study is that it was carefully, thoughtfully, and accurately drafted. After careful review, it is clear that the presentation benefited greatly from the comments of the external reviewers. In particular, the comparative aspect of this case study was quite interesting. While DecaBDE and MWCNT share little in the way of physicochemical properties, their comparison from a use-to-exposure life cycle perspective adds value to the case study. I believe that this is particularly true in the case of MWCNT, for which very few real measures of exposure and/or environmental occurrence have been made (in contrast to DecaBDE). However, inclusion of detailed direct comparison between these materials within the main body of the CEA document would have been unnecessarily tedious and distracting from the primary goal of the case study. The decision to move most of the DecaBDE-relevant information to the appendix was well-founded, and the inclusion of comparative "text boxes" within the main text body are useful. I am unsure that MWCNTs will ever find widespread use in flame retardant application (this is still a niche use with only one example and a few literature citations), so the focus on this particular incarnation of MWCNT use is dubious. I find that the research priority areas for MWCNT identified during the prioritization process are indeed very important and relevant, but there is some inconsistency. In particular: "ecological impacts of MWCNT in aquatic biota" was identified as a priority area, but both exposure and dose of MWCNT in ecological populations were not identified as priority. These aspects of MWCNT behavior are intimately linked and it seems inappropriate to separate their priorities.

Fadri Gottschalk

This document is a very thorough, well-written scientific report that reflects the extensive work done by the authors.
The report is substantial and thus requires much time reading but also to reflect on its contents. It covers—with exceptions (commented in detail below)—the relevant research, and shows that the CEA (Comprehensive Environmental Assessment) approach for analyzing the environmental implications of chemicals or engineered nanomaterial necessitates much effort on the part of the researchers; however, it may produce new evidence by combining literature knowledge with judgments of experts and other involved people.

The report, as a whole, is somewhat awkwardly organized, with many annotations and numerous text boxes, tables, and figures both in the text and appendices. I have some general points to mention—this is mostly more a wish list than a list of absolute necessities—that hopefully help the authors conduct their final edits to the report.

A. Shorten many lengthy passages distributed throughout the document, and clearly present at the beginning what work methods (embedded in CEA) contributed to this manuscript: literature review, online questioning, expert workshop, first-stage peer review, etc.

B. The reader often does not see any difference between the main text and the appendices. In both categories, the text (sometimes with similar if not the same content), tables, and even text boxes within the appendices, are dense. For me, the annexed material contains information that is important enough to be included in the body of the manuscript. Thus, I would reorganize the main copy and the appendices by keeping, for example, most of the text in the body and only tables with more or less just literature data and other documentation into the appendices. Furthermore, some text (especially some introductions to particular chapters) in the appendices seems repetitious of the corresponding introductions in the main text.

C. The manuscript may work very well in electronic form, but as a paper document only, some difficulties are present: for example, it lacks the page numbers in the table of contents (precise numbers and chapter independent page numbers).

D. I know there is a limit to how much literature research one can do and include, but I've indicated below where there is a lack of literature (for the time period of your data search). Including it may benefit your report.

E. I found it somewhat tedious to be faced with so many intra-textual references (from back to front) to chapters that I had already read. However, these might make more sense to readers of the electronic version.

F. Research priorities were identified through the RTI workshop process and presented in a satisfactory manner in the report; however, I wonder if in this workshop quantitative parameter values were also produced that could be used directly for environmental exposure or effect assessments/modeling. Could you add a chapter, some passages, on

questions such as how to organize/use expert workshops for data preparation of multimedia modeling? In addition, the reader seems to be left somewhat in the dark regarding the 13 participants in the workshop—for example, were the participants experts in all areas discussed in the workshop?

G. We know (as suggested in the first review process), that the comparison with decaBDE may either confuse or help the reader. The arguments for and against such comparison were presented in the first review. I would like to mention the "DecaBDE Can Inform MWCNT Assessment" boxes: these boxes and their idea convince me, but maybe you could be more specific when presenting the differences (and their consequences for the assessment) between these semi-volatile molecules and the carbon particles. Such clear distinction could help modelers and experimental/analytical people in using/defining the right parameters and using the right model input values.

H. I'm aware this report is not intended to serve as a basis for near-term risk decisions on the use of MWCNTs. As mentioned above, research priorities were clearly identified via this CEA. However, I wonder if from such great efforts we should not get some kind of risk results as well. The authors were very cautious and did not draw any conclusions in the context of risk estimation/evaluation. There are good reasons to be very careful, but some prudent first/rough assessments (or some references to risk results presented elsewhere) could probably be presented.

Stig I. Olsen

The document is well structured and cross-referencing links within the document are a highly appreciated feature. Overall, the accuracy is good (to my knowledge). Clarity of presentation sometimes suffers due to the length of the text; however, often the information is also presented in an overview in tables which is very good. But it would also be good to summarize after each chapter.

The whole process of the CEA is thoroughly described and provides a very good introduction to the remainder of the document, as well as to the terminology used. Also, the previous steps of the current document are adequately described and give the reader a good understanding of why the document is built as it is. However, a good understanding of the framework, as such, was for me better achieved after reading Chapters 6.1 and 6.2.

Figure 1-3 provides a very good overview of the results of the collective judgment prioritization process.

The relatively long introduction and explanation of flame retardancy is not at all times very relevant to CEA—I would reduce it to a few pages explaining the principles of MWCNT for flame retardancy and providing the perspectives of potential volumes and thus releases—and put the remainder in an appendix.

Additional highlight boxes work well in conveying the additional information and are in most instances relevant.

It is a bit confusing that LCA is mixed up a bit with risk assessment—it is clear that e.g. the feedstock may not be of importance for risk assessment of MWCNT, but in an LCA it can be of importance due to other types of emissions, resource usage, etc. Likewise in the manufacturing, there will be extensive use of solvents to refine the MWCNT or reagents for functionalization—which are not taken into account in the CEA (except to a minor extent in Chapter 4.5 "cumulative exposures") but would be in an LCA (as well as the waste material/by-products from the refining). It is stressed several times, e.g. on page 5.1 lines 3-7, that the CEA framework includes other impacts than toxicological—however, this is not at all well communicated in the document as a whole. The whole Chapter 2 on the product life cycle could have put a lot more weight on these issues rather than just being briefly mentioned in Chapter 5.3.

Areas in which there is no information are often not mentioned, i.e. it should be clearly stated that in order to actually do an assessment we would need this information. An example is Chapter 3.3 where nothing is mentioned about stability and transformation in water and sediment.

The conclusions are generally sound.

V. RESPONSE TO CHARGE QUESTIONS

Completeness and Accuracy

Charge Question 1
Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

Karin Aschberger

The science is, in general, accurately and clearly conveyed throughout the document.

I consider that the data discussed in this document have been retrieved from the latest peer-reviewed scientific papers and most accurate reviews. However, there are some specific areas and references that can be extended and included.

References (often not the original references, but those of reviews. I can only refer to those that I know very well):

- Table 1-8: ECB 2003: EU Risk Assessment Report as reference for DecaBDE phys-chem properties; and

- Table 1-9: Johnston and Aschberger as references for MWCNT phys-chem properties. Please refer to original sources, where these properties have been determined.

Be consistent with references. For example, in Text Boxes 5-1 (but also others), only part of the text is referenced. Either give references for all statements or no references in text boxes and only in the accompanying text.

Additional relevant information sources on MWCNTs could be considered:

- There is a REACH registration dossier on MWCNT (for Baytubes and Nanocyl), parts of which are publicly available. It contains, for example, information on TG GLP studies which were not published in peer-reviewed papers. This information could be used to fill gaps in Table 5-1 and the corresponding text. Link: http://apps.echa.europa.eu/registered/data/dossiers/DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031/DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031_DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031.html

  It also gives rough information on manufacturing volume, as they were registered for the tonnage volume: 100-1000 tons/year.

- The Japanese Risk Assessment of Manufactures Nanomaterials – CNT (NEDO project):

Nakanishi, J., Ed. Risk assessment of manufaucured nanomaterials: Carbon nanotube (CNT). Final report issued on August 12, 2011. NEDO project (P06041) Research and development of nanoparticle characterization methods. Link: http://www.aist-riss.jp/main/modules/product/nano_rad.html?ml_lang=en

- Human Health Hazard Assessment and Classification of Carbon Nanotubes. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Safe Work Australia. October 2012. ISBN 978 0 642 78542 8 [Online PDF]. Link: http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/human-health-hazard-assessment-and-classification-of-carbon-nanotubes

I disagree with the following statements in Chapter 5:

5-10: Subchronic – chronic systemic toxicity

The way it is presented it seems that there are no subchronic/chronic studies (by any route) available – or no studies testing systemic effects. (In vivo) - Studies are not made separately for local or systemic effects, but they can be observed and/or reported. There are two subchronic inhalation studies with MWCNTs available which have not reported systemic effects. In addition, the Pauluhn study included a 6 M post-exposure observation period – this could be added where the study is described.

5-14: Relevance of in vitro data

The introductory sentence should be revised.

There is a general requirement to replace animal studies by alternative methods and some in vitro test are validated and regularly used in regulatory risk assessment: mutagenicity (usually only in vivo confirmation of positive in vitro results), dermal absorption, and skin and eye irritation. A good overview on the suitability of in vitro methods (not validated for NM yet) for NM hazard assessment are given in:

- SCCS 2012: Guidance on the safety assessment of nanomaterials in cosmetics. Link: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_005.pdf

- Hartung et al. 2011. Alternative in vitro assays in nanomaterial toxicology. Link: http://onlinelibrary.wiley.com/doi/10.1002/wnan.153/abstract;jsessionid=DF763EC777E464BDF520FF2C46822C6C.d03t03

Several EU framework projects are focusing on development of alternative methods for NM toxicity testing, in vitro-in vivo extrapolation (e.g., ITS-Nano, MARINA, ENPRA).

Further information on in vitro data and alternative methods to support toxicological studies can be found in:

- Adler, S., D. Basketter, et al. (2011). Alternative (non-animal) methods for cosmetics testing: current status and future prospects-2010. Archives of toxicology 85(5): 367-485.

- Hartung, T., B. J. Blaauboer, et al. (2011). An expert consortium review of the EC-commissioned report "alternative (Non-Animal) methods for cosmetics testing: current status and future prospects - 2010". ALTEX 28(3): 183-209.

Jaclyn Cañas-Carrell

To the best of my knowledge, I believe the science is accurately conveyed throughout the document. No revisions are needed. The extensive review of the science and document that preceded this current review has resulted in a well written and accurate version of the final document.

P. Lee Ferguson

In general, I have found that the authors and the external reviewers have done an admirable job of summarizing the latest research findings concerning the state of the science regarding MWCNT fate, exposure, and effects. In particular, while there is broad consensus for certain properties and behaviors of MWCNTs in the environment (e.g., their tendency to aggregate and to associate with particulates in aqueous systems), others are more controversial (e.g., potential for bioaccumulation or ability to cross cell membranes). These areas of respective clarity or lack thereof are very important to identify in a case study describing materials for which fate/transport models based on physicochemical properties are of limited relevance. I believe that this aspect was well described in the case study. I do feel that the entire case study suffers from a relatively narrow focus on MWCNT. In many cases, SWCNT may behave in a very similar fashion to MWCNT in environmental and biological systems, and I feel that the case study would have benefited from inclusion of the relevant research (e.g. fate and transport, analytical methods, exposure predictions) related to SWCNT also. As noted in the document, SWCNT may also be used in textile applications and will therefore experience many of the same routes-of-entry to the environment. Risk assessment of the (likely) more plentiful MWCNT may be informed by research that is relevant to BOTH classes of CNT, including the (likely) lower production-volume SWCNT.

Fadri Gottschalk

Yes, absolutely; my impression was that the authors accurately conveyed the science considered. Several spot checks on the literature I'm well familiar with did not show any inaccuracies.

I've got two critical points:

1. <u>Completeness</u>: I'm not saying that you have to take everything into account, but I collected the literature that I thought missing and indicated where I would place/consider such literature in the

report. See below (**A**) for missing literature.

2. In the context of the comparison of MWCNT to decaBDE (i.e., justification for such a comparison), I would pay more attention to the complex issues of fate that we are faced with when assessing the environmental distribution of nanomaterials, as described several times (Christian et al. 2008; Hassellöv et al. 2008; Klaine et al. 2008; Tiede et al. 2008).

The pros and cons in comparing MWCNT to decaBDE have been comprehensively mentioned in the first review process and I do not want to repeat this; the responses/adaptations of the authors satisfy so far. However, I'm still missing a kind of introductory (immediate) explanation also from a material property perspective (well placed at the beginning, for example, in Chapter 1.1.4, Selection of DecaBDE for Comparison) as to why the comparison of MWCNT to decaBDE can be useful. It is somehow incomplete to focus on a comparison that exclusively helps identify research gaps by illustrating the manufacturing process and exposure scenarios and by understanding the process of regulating a chemical, etc.

In this context, I also wonder if the "partner chapters" G and H should be chapters of the appendices or moved to the main text. I guess you could build these two chapters in a more congruent way or rather exactly with the same structure. This would highlight similarities, differences in material properties, and data gaps. For example, in Chapter H.3.3.1, water solubility and Kow are said to be important physicochemical factors for predicting the behavior of BDE-209 in water. I agree, and of course the Kow is not applicable to non-soluble MWCNTs. Now the equivalent chapter for MWCNTs in Chapter G is not really there; however, discussion/literature on the crucial parameter "fate of carbon nanotubes" in water is not totally missing (see also literature suggestions made). Regarding Table H-3: an equivalent table—even if partially empty—for MWCNTs in Chapter G would be very interesting.

A. <u>Literature that one should check for possible consideration (till November 2012)</u>

A.1) Environmental fate (Chapter 1.1.4, see point 2 just mentioned above):

Hassellov, M., Readman, J.W., Ranville, J.F., Tiede, K., 2008. Nanoparticle analysis and characterization methodologies in environmental risk assessment of engineered nanoparticles. Ecotoxicology 17, 344-361.

Klaine, S.J., Alvarez, P.J.J., Batley, G.E., Fernandes, T.F., Handy, R.D., Lyon, D.Y., Mahendra, S., McLaughlin, M.J., Lead, J.R., 2008. Nanomaterials in the environment: Behavior, fate, bioavailability, and effects. Environmental Toxicology & Chemistry 27, 1825-1851.

Tiede, K., Boxall, A.B.A., Tear, S.P., Lewis, J., David, H., Hassellov, M., 2008. Detection and characterization of engineered nanoparticles in food and the environment. Food Additives and Contaminants 25, 795-821.

A.2) MWCNTs use in flame-retardant textiles (Chapters 1.3.2, 1.3.3):

Fasfous, I.I., Radwan, E.S., Dawoud, J.N., 2010. Kinetics, equilibrium and thermodynamics of

the sorption of tetrabromobisphenol A on multiwalled carbon nanotubes. Applied Surface Science 256, 7246-7252.

Haiou, Y., Jie, L., Xin, W., Zhiwei, J., Yujie, W., Lu, W., Jun, Z., Shaoyun, F., Tao, T., 2011. Charing polymer wrapped carbon nanotubes for simultaneously improving the flame retardancy and mechanical properties of epoxy resin. Polymer 52, 4891-4898.

Haiou, Y., Jie, L., Zhe, W., Zhiwei, J., Tao, T., 2009. Combination of carbon nanotubes with Ni 2O 3 for simultaneously improving the flame retardancy and mechanical properties of polyethylene. Journal of Physical Chemistry C 113, 13092-13097.

Im, J.S., Bai, B.C., Bae, T.-S., In, S.J., Lee, Y.-S., 2011. Improved anti-oxidation properties of electrospun polyurethane nanofibers achieved by oxyfluorinated multi-walled carbon nanotubes and aluminum hydroxide. Materials Chemistry and Physics 126, 685-692.

Ji Sun, I., Byong Chol, B., Tae-Sung, B., Se Jin, I., Young-Seak, L., 2011. Improved anti-oxidation properties of electrospun polyurethane nanofibers achieved by oxyfluorinated multi-walled carbon nanotubes and aluminum hydroxide. Materials Chemistry and Physics 126, 685-692.

Lee, S.K., Bai, B.C., Im, J.S., In, S.J., Lee, Y.-S., 2010. Flame retardant epoxy complex produced by addition of montmorillonite and carbon nanotube. Journal of Industrial and Engineering Chemistry 16, 891-895.

Qiu, J., Zhang, S.-h., Wang, G.-j., Gong, Y.-l., 2009. Surface modification and application of multi-walled carbon nanotubes in fire-retardant coatings. New Carbon Materials 24, 344-348.

Ullah, S., Ahmad, F., 2012. Enhancing the Char Resistant of Expandable Graphite Based Intumescent Fire Retardant Coatings by using Multi-wall Carbon Nano Tubes for Structural Steel. Diffusion and Defect Data Part B (Solid State Phenomena) 185, 90-93.

Verdejo, R., Barroso-Bujans, F., Rodriguez-Perez, M.A., de Saja, J.A., Arroyo, M., Lopez-Manchado, M.A., 2008. Carbon nanotubes provide self-extinguishing grade to silicone-based foams. Journal of Materials Chemistry 18, 3933-3939.

Wang, J.-X., Jiang, D.-Q., Gu, Z.-Y., Yan, X.-P., 2006. Multiwalled carbon nanotubes coated fibers for solid-phase microextraction of polybrominated diphenyl ethers in water and milk samples before gas chromatography with electron-capture detection. Journal of Chromatography A 1137, 8-14.

Outside the review time range:

Knight, C.C., Ip, F., Zeng, C., Zhang, C., Wang, B., 2013. A highly efficient fire-retardant nanomaterial based on carbon nanotubes and magnesium hydroxide. Fire and Materials 37, 91-99.

A.3) Production volumes estimations of raw material (Chapter 2):

Piccinno F, Gottschalk F, Seeger S, Nowack B. Industrial Production Quantities and Uses of Ten Engineered Nanomaterials in Europe and the World. J Nanopart Res. 2012; 14.

Future Markets. The World Market for Carbon Nanotubes, Nanofibers, Fullerenes and POSS. Future Markets, Inc.; 2011.

A.4) Material synthesis (Chapter 2.2.2), these are all review articles:

Ying, L.S., Salleh, M.A.b.M., Yusoff, H.B.M., Rashid, S.B.A., Abd Razak, J.B., 2011. Continuous production of carbon nanotubes - A review. Journal of Industrial and Engineering Chemistry 17, 367-376.

Golnabi, H., 2012. Carbon nanotube research developments in terms of published papers and patents, synthesis and production. Scientia Iranica 19, 2012-2022.

Huang, J., Zhang, Q., Zhao, M., Wei, F., 2102. A review of the large-scale production of carbon nanotubes: The practice of nanoscale process engineering. Chinese Science Bulletin 57, 157-166.

Yanfeng, M., Bin, W., Yingpeng, W., Yi, H., Yongsheng, C., 2011. The production of horizontally aligned single-walled carbon nanotubes. Carbon 49, 4098-4110.

Kumar, M., Ando, Y., 2010. Chemical Vapor Deposition of Carbon Nanotubes: A Review on Growth Mechanism and Mass Production. Journal of Nanoscience and Nanotechnology 10, 3739-3758.

A.5) Releases during the material synthesis/handling (Chapter 2.2.2.2):

Ogura, I., Sakurai, H., Mizuno, K., Gamo, M., 2011. Release potential of single-wall carbon nanotubes produced by super-growth method during manufacturing and handling. Journal of Nanoparticle Research 13, 1265-1280.

A.6) Releases during use (Chapter 2.4.2.):

Schlagenhauf, L., Chu, B.T.T., Buha, J., Nueesch, F., Wang, J., 2012. Release of Carbon Nanotubes from an Epoxy-Based Nanocomposite during an Abrasion Process. Environmental Science & Technology 46, 7366-7372.

Liang, S., Chen, G., Peddle, J., Zhao, Y., 2012. Reversible dispersion and releasing of single-walled carbon nanotubes by a stimuli-responsive TTFV-phenylacetylene polymer. Chemical Communications 48, 3100-3102.

A.7) Waste handling, incineration (Chapter 2.5.2.):

Walser, T., Limbach, L.K., Brogioli, R., Erismann, E., Flamigni, L., Hattendorf, B., Juchli, M.,

Krumeich, F., Ludwig, C., Prikopsky, K., Rossier, M., Saner, D., Sigg, A., Hellweg, S., Guenther, D., Stark, W.J., 2012. Persistence of engineered nanoparticles in a municipal solid-waste incineration plant. Nature Nanotechnology 7, 520-524.

Mueller NC, Buha J, Wang J, Ulrich A, Nowack B. Modeling the flows of engineered nanomaterials during waste handling. Environmental Science: Processes & Impacts. 2013; 15(1): 251-9.

A.8) Fate in water (Chapter 3.3.):

Schwyzer I, Kaegi R, Sigg L, Smajda R, Magrez A, Nowack B. Long-term colloidal stability of 10 carbon nanotube types in the absence/presence of humic acid and calcium. Environmental Pollution.2012; 169(0): 64-73.

A.9) Ecotoxicological effects (Chapter 5.2.):

Zhu Y, Zhao Q, Li Y, Cai X, Li W. 2006. The interaction and toxicity of multi-walled carbon nanotubes with Stylonychia mytilus. J. Nanosci. Nanotechnol. 6:1357-1364.

Ghafari P, St-Denis CH, Power ME, Jin X, Tsou V, Mandal HS, Bols NC, Tang XW. 2008. Impact of carbon nanotubes on the ingestion and digestion of bacteria by ciliated protozoa. Nature Nanotechnology 3:347-351.

Schwab F, Bucheli TD, Lukhele LP, Magrez A, Nowack B, Sigg L, Knauer K. 2010. Are Carbon Nanotube Effects on Green Algae Caused by Shading and Agglomeration? Environmental Science & Technology 45:6136-6144.

Templeton RC, Ferguson PL, Washburn KM, Scrivens WA, Chandler GT. 2006. Lifecycle effects of single-walled carbon nanotubes (SWNTs) on an estuarine meiobenthic copepod. Environ. Sci. Technol. 40:7387-7393.

Roberts AP, Mount AS, Seda B, Souther J, Qiao R, Lin S, Ke PC, Rao AM, Klaine SJ. 2007. In vivo biomodification of lipid-coated carbon nanotubes by Daphnia magna. Environ. Sci. Technol. 41:3025-3029.

Cheng JP, Flahaut E, Cheng SH. 2007. Effect of carbon nanotubes on developing zebrafish (Danio rerio) embryos. Environ. Toxicol. Chem. 26:708-716.

A.10) Analytical methods for detecting, measuring, and characterizing (Appendix B):
(I know, fullerenes are not really CNT and the studies are not without controversy, but, since there's nothing else for comparison/analogies?)

Farré, M., Pèrez, S., Gajda-Schrantz, K., Osorio, V., Kantiani, L., Ginebreda, A., Barcelü, D., 2010. First determination of C60 and C70 fullerenes and N-methylfulleropyrrolidine C60 on the suspended material of wastewater effluents by liquid chromatography hybrid quadrupole linear ion trap tandem mass spectrometry. Journal of Hydrology 383, 44-51.

Sanchis, J., Berrojalbiz, N., Caballero, G., Dachs, J., Farre, M., Barcelo, D., 2011. Occurrence of Aerosol-Bound Fullerenes in the Mediterranean Sea Atmosphere. Environmental Science & Technology 46, 1335-1343.

Stig I. Olsen

Generally, I find that the science is accurately conveyed. A few comments to Chapter 5 are:

Page 5-29 - the review of Eckelman et al. (2012) lacks the essential information that, when applying the USEtox framework, the authors make adaptations in order to handle the CNTs. USEtox is developed for organic chemicals and will probably not be suitable for CNTs. This could be a factor to consider in their results.

In Chapter 5.3.3, I don't necessarily think there is an unclear relationship between climate change and production of MWCNT. The high CO2 in Khanna et al. is due to the energy consumption and, considering the high energy consumption listed earlier, there will be huge climate change impacts related to all production pathways.

Chapter 6.3.4.4 lacks reflections on the gaps in knowledge regarding broad environmental considerations (life cycle assessments).

Clarity and Use of Priority Areas to Support Research Planning

Charge Question 2
Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

Karin Aschberger

Priority areas can be clearly identified as they are clearly highlighted throughout the document. The presentation of the division of importance and confidence ranking (and associated colours) is considered useful, especially the confidence because it plays an important role in the regulatory decision making. For example, in Chapter 4, Section 4.2 Human Exposure and Kinetics Leading to Dose, priority research areas identified inhalation exposure route as the highest priority area, followed by ingestion and dermal exposure. This information is supported by the literature presented.

In each subsection, exposure scenarios sorted by exposure route (inhalation, oral, and dermal) are presented for the occupational scenarios. For clarity, a summary table of this information highlighting the activities related to each kind of exposure with exposure levels data (if available) is suggested for:

- Synthesis, Processing, and Handling.
- Formulation of Flame Retardant, Application to Textiles, Upholstering.
- Storage of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products.
- Disposal and Recycling of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products.

Additional Comments:

- The identified priority areas for Human Health are in accordance with our findings within the ENRHES (http://ihcp.jrc.ec.europa.eu/whats-new/enhres-final-report) and the currently running ITS-Nano FP7 project (http://www.its-nano.eu/). For the Environment, there is a different view on the terrestrial compartment. It was identified as priority research area under ENRHES and ITS-Nano. Sediment and soil are usually sinks for NM (e.g., see our paper: Aschberger. Environment International 37 (2011) 1143–1156).

Sedimented NM in wastewater, which was also identified as priority, could end up in soil together with sludge.

- In general, reasons for not prioritized areas could be better explained (e.g., terrestrial environment).

Jaclyn Cañas-Carrell

Yes, the Priority Research Areas are clearly identified throughout the document. Putting the Priority Research Areas in text boxes really highlights the priority areas. In addition, the discussion of each Priority Research Area in Chapter 6 helps to further emphasize the areas and provides an overall succinct summary of the research needs related to MWCNTs in flame-retardants.

P. Lee Ferguson

The priority areas are very clearly indicated in the document, starting with Figure 1-3 and continuing with highlighted boxes within the main body of the text. In particular, I find the "color-coding" of the boxes within the document easy to follow and helpful.

Fadri Gottschalk

Yes. Basically, priority research areas are highlighted very well in the report. The text boxes throughout are well organized and color-coded: red refers to the so-called priority areas for research, grey to unprioritized areas, and green boxes are used for the decaBDE–MWCNT comparison. However, numbering and indexing for those boxes is missing, making it difficult to read the report as a hard copy.

The Importance/Confidence Matrices are clear and easy to understand. But I wonder if a more detailed textual analysis of these matrices' based output would provide the basis for a research paper to be extracted from this report. Unfortunately, having only 13 participants is not enough for statistical evaluation, and the competences of the participants are not really discussed. Furthermore, I'm not sure whether it makes sense that the authors only present in Chapter 6—Chapter 6.3, with the participants' rationale for designating the areas, shows the outcomes of the prioritization process in more detail—the identification of these priority areas by expert stakeholders that in the end represents the crucial part for connecting risk research, assessment, and management. Since these outcomes have been used to focus the information in the whole case study, should this information not be included as a key part of the report already at the beginning?

Another point is that even if the additional information highlight boxes (with scientific concepts related to the priority areas), as well as the other figures and tables, refer to priority research areas (Boxes 6 and 7 refer, for example, explicitly to issues covering such areas), the organizational relationship between the different boxes (figures and tables) seems to me not too apparent in the report. A table description with reference to the areas, for example, for Table 6-3, and directly appended to the table (and not only in the main text body), would help. The same

kind of intra-textual references/indications on the interconnections are also needed for the green boxes, since these boxes reveal how data on decaBDE should be used for MWCNT research planning that is focused on these priority areas.

Stig I. Olsen

I find that the boxes presenting "prioritized" or "unprioritized" research areas are very illustrative and very clearly highlight the opinions of previous experts.

Clarity and Use of Priority Areas to Support Research Planning

Charge Question 3
For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

Karin Aschberger

Please find some additional references below and in the Specific Observations section (not exhaustive, as I didn't have time to check everything carefully):

Studies on release of polymer bound CNTs (it seems that not much information has been included in the report):

- Wohlleben et al. 2011. On the lifecycle of nanocomposites: comparing release fragments and their in vivo hazards from three release mechanisms and four nanocomposites. Small. No 16, 2384-2395.

- Wohlleben et al. 2013. Elastic CNT-polyurethane nanocomposite: synthesis, performance and assessment of fragments released during use. Nanoscale 369-380

- Stahlmecke et al. (IUTA Duisburg Germany) 2013. Investigations on the possible CNT release at the end-of-Life of CNT-composites. Poster (not found on internet, but could be made available to you).

- Ogura et al. (AIST, TASC Japan) 2012. Potential release of carbon nanotubes from their composites during grinding. Poster at nanosafe 2012: http://www.certh.gr/dat/A974408A/file.pdf

- Movahedi, Alireza 2008. Risk assessment of nanoparticle release from the structure of polymeric nanocomposites – Master Thesis University Goteburg: http://libris.kb.se/bib/12060839

Environmental Fate:

- O'Carroll, D. M., Liu, X., Mattison, N. T., Petersen, E. J. 2013. Impact of size on carbon nanotube transport in natural porous media. *Journal of Colloid & Interface Science*, 390(1), 96-104.

- Zhang, L., Petersen, E. J., Zhang, W., Chen, Y. S., Cabrera, M., Huang, Q. 2012. Phase distribution of 14C-labeled multi-walled carbon nanotubes in aqueous systems containing model solids: clay. *Environmental Pollution*. 166, 75-81.

- Liu, X., O'Carroll, D.M., Petersen, E.J., Huang, Q., Anderson, L. 2009. Mobility of multi-

walled carbon nanotubes in porous media. Environmental Science & Technology. 43, (21), 8153-8158.

Ecotoxicity:

- Petersen, E. J., Pinto, R. A., Mai, D. J., Landrum, P. F., Weber, W. J., Jr. 2011. Influence of Polyethyleneimine Graftings of Carbon Nanotubes on their Accumulation and Elimination by and Toxicity to *Daphnia magna*. *Environmental Science and Technology*. 44, (3), 1133-1138.

- Galloway, Tamara, et al. "Sublethal toxicity of nano-titanium dioxide and carbon nanotubes in a sediment dwelling marine polychaetes." *Environmental Pollution* 158.5 (2010): 1748-1755. **(NB! SWCNT & marine sediment!!!). NOEC > 0.03 g/kg to** *A*renicola marina (lugworm)

Bioaccumulation:

- Petersen, E. J., Pinto, R. A., Mai, D. J., Landrum, P. F., Weber, W. J., Jr. 2011. Influence of Polyethyleneimine Graftings of Carbon Nanotubes on their Accumulation and Elimination by and Toxicity to *Daphnia magna*. *Environmental Science and Technology*. 44, (3), 1133-1138.

- Petersen, E. J., Akkanen, J., Kukkonen, J. V. K., Weber, W. J., Jr. 2009. Biological Uptake and Depuration of Carbon Nanotubes by *Daphnia magna*. Environmental Science & Technology. 43, (8), 2969-2975.

Jaclyn Cañas-Carrell

There are two additional studies that could be considered for inclusion to support the Priority Research Areas:

1. Irin et al. (2012) is listed in Highlight Box 10 but not listed in the tables in Appendix B.

    a. Irin, F, B Shrestha, JE Cañas, M Saed and MJ Green. 2012. Detection of carbon nanotubes in plant roots through microwave-induced heating. Carbon 50:4441-4449.

2. Li et al. (2013) could be added to pp. 6-24, line 30. This paper demonstrated no substantial uptake of MWCNTs in earthworms in soil.

    a. Li, S, F Irin, FO Atore, MJ Green, and JE Cañas-Carrell. 2013. Determination of carbon nanotube bioaccumulation in earthworms measured by a microwave-based detection technique. Science of the Total Environment, In press. doi: 10.1016/j.scitotenv.2012.12.037.

P. Lee Ferguson

After carefully reviewing the list of references, the descriptions of previous studies and their conclusions, and performing independent literature searches, I believe that the case study has accurately represented the most relevant research findings that can provide guidance for future research supporting risk management of MWCNT. I do not know of any MWCNT-specific studies that have been omitted from the case study. However, as I note above, I believe that the authors and external reviewers missed an opportunity by explicitly excluding environmental fate, transport, and effects data for SWCNT (especially with regard to aquatic fate and mechanisms of human/aquatic toxicity). SWCNT may be expected to behave in very similar ways to MWCNT in the environment (based on similarity of their physicochemical properties) and thus a more complete CEA might have been conducted on "CNT in textiles", irrespective of their intended function in the textile (e.g., flame-retardant vs. stain repellent). In fact, this approach would be quite defensible in light of the fact (as indicated in the box on page 1-28) that MWCNT use as flame retardant coatings in textiles is not yet widespread and is not anticipated to increase dramatically in the future.

Fadri Gottschalk

Please see the literature suggestions made above under Question 1 that have been grouped by the different research areas.

Stig I. Olsen

I think that the incineration part (Chapter 2.5.2.2) is relying too much on anticipation that MWCNT will be oxidized in incineration. A few papers I have (included at the bottom of this review) do not clearly indicate that this is so. And even controlled incineration has clumps of waste that are not fully incinerated or where the temperature does not reach maximum.

Clarity and Use of Priority Areas to Support Research Planning

Charge Question 4
Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

Karin Aschberger

The document is mainly focusing on the research areas but does not include recommendations on how this could be achieved. In addition to increasing the knowledge about MWCNTs or NM in general, there should be also focus on better exploitation of existing data, reading across and the use of alternative methods (in vitro/QSAR).

The consideration of other impacts such as energy, climate change, economics etc., is appreciated. As mentioned above, it should be considered that MWCNT alone will not be sufficient to replace DecaBDE.

Jaclyn Cañas-Carrell

The document definitely supports research planning to inform future risk assessments. The questions outlined at the end of the green text boxes (DecaBDE Can Inform MWCNT Assessment) are very helpful to outline research needs. In addition, the Priority Research Area text boxes (and Unprioritized Research Areas) also helped to outline research needs. Chapter 6 is also instrumental in providing further discussion to inform research planning.

With the exception of the Impacts Priority Research Area for Aquatic Biota (p. 5-19), the other text boxes clearly define research gaps and questions to ask. After reading Chapter 6.3.4.3, particular research needs are more apparent. This particular text box could be improved to include what is discussed in Chapter 6.3.4.3.

P. Lee Ferguson

With the exception of some discontinuities in research priorities (e.g., the identification of "ecological impacts of MWCNT in aquatic biota" as a priority area, while classifying both exposure and dose of MWCNT in ecological populations as lower priority), I found that the document was generally very well structured to guide future research in the area of environmental and health implications of MWCNT. One admirable aspect of this case study is that the environmental and (especially aquatic) exposure/transport/effects characteristics discussed for MWCNT in Chapters 3-5 are relevant for more than just the potential release from use in flame-retardants on textiles. Therefore, the predictions, prioritization, and implications will be valid for MWCNT releases to the environment under a variety of scenarios. Conversely, I find that the weakest part of the document is Chapter 2 (Product Life Cycle), since much of it is focused exclusively on the use of MWCNT in the very narrow application of flame retardants in textiles.

Fadri Gottschalk

Yes, this goal is achieved. However, it will be important to evaluate the missing literature (please see the comments above, Charge Question 1) to exclude that, until now, not considered (possibly conflicting) results would inform research planning differently. Second, at the end of the green boxes, concrete research questions are listed in each case to inform MWCNT research planning in the identified priority areas. I'm wondering if it would make sense to collect and prioritize all these concrete questions/instructions for researchers in a summary or conclusion table, box, or figure. The same question arises for all conclusions made on research planning outside of the comparison of decaBDE to MWCNT.

Stig I. Olsen

I find that the document is very supportive in future research planning. Chapter 6 makes a good conclusion on the process.

In Chapter 5 it would be very helpful to have a table that better summarizes the studies mentioned in the text. Table 5-1 is not very helpful (it almost says there are no data on anything) since there are useful results from a range of studies. Tables 5-2 and 5-3 convey much more useful information.

Clarity and Use of Priority Areas to Support Research Planning

Charge Question 5
Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

Karin Aschberger

The document organization is logical although sometimes it is repetitive and could be shorter in some parts. The extended executive summary relating to the different chapters gives a clear overview on the content of the document and helps to focus on specific areas.

In my opinion, within Chapter 4, a better separation between human and environmental exposure scenarios and data would be helpful. This separation is achieved in Chapter 5, in which the information on potential human health and ecological impacts of CNTs are well divided in two subsections (5.1. Human Health Effects and 5.2. Ecological Effects).

Jaclyn Cañas-Carrell

The organization of the document is excellent. It flows in a logical manner and is easy to understand, at least to someone with a toxicology background and that does nanotoxicology research. While I cannot speak from the perspective of someone with less background, I believe the document does a good job in defining key concepts or ideas for those perhaps not as versed in toxicology or nanotoxicology.

P. Lee Ferguson

I've reviewed both the Draft for External Review and the current (revised) Case Study, and I find that the use of information boxes, DecaBDE/MWCNT-comparison boxes, and priority-area boxes throughout the text has greatly improved the logical flow of the document. I do, however, believe that Section 1.1 is unnecessarily verbose and might be better suited to an appendix. Also, Appendix J (Knowledge Maps) – if used at all – would be much more effective as part of the main body of text, perhaps in Chapter 6.

Fadri Gottschalk

As partially mentioned in my introductory comments, I would suggest the authors look at:

- numbering and indexing all chapters, boxes, tables, and figures
- creating more transparent and consistent organization regarding the alternating between decaBDE and MWCNT in the text and document structure, which at present seems discordant
- numbering and indexing all pages in the hard copy
- declaring explicitly and at the beginning of this manuscript how the authors distinguish between content for Appendices E and F and Chapter 3; Appendix F and Chapters 4 and

5; Appendices G, H, and Chapter 6; and Appendix G and Chapters 2–5

- explicitly declaring at the beginning of the manuscript the use and purpose of the different kinds of boxes
- condensing the annotations and possibly moving relevant annotated text (as proposed above) into the main document
- condensing lengthy passages
- removing any extraneous cross-references in the text between the chapters, especially when later chapters refer back to earlier ones

Stig I. Olsen

The overall structure is logical. However, as previously mentioned, I find that the information in Chapters 6.1 and 6.2 would be better placed in Chapter 1 to give a better understanding of the purpose of the document.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

Charge Question 6
Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

Karin Aschberger

Comments are transparently addressed.

Jaclyn Cañas-Carrell

Yes, peer and public stakeholder comments are clearly summarized and conveyed through the use of tables. After looking at Tables I-12 through I-14, it appears that comments are clearly summarized in Tables I-4 through I-9 and I-11. No further revisions are necessary.

P. Lee Ferguson

Yes – I have almost no comments on this aspect of the case study. Appendix I is somewhat difficult to follow, but it is well-organized and cross-referenced among reviewer comments, agency responses, and document edits/amendments. In general, the revisions were made in a very thoughtful and systematic manner.

Fadri Gottschalk

Yes.

Stig I. Olsen

They are comprehensively and transparently conveyed.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

Charge Question 7
Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

Karin Aschberger

Comments are transparently and clearly conveyed. The double presentation of original comments and summarized comments make it very transparent.

Jaclyn Cañas-Carrell

Yes, EPA responses to comments are also transparently and clearly conveyed through the use of tables. EPA responses are detailed with specific sections, Priority Research Area Boxes, or Highlight Text Boxes where revisions were incorporated as suggested. In addition, EPA responses were fully justified in the few cases where no change was made.

P. Lee Ferguson

As above – yes, the responses to comments are also very well-described in Appendix I. I have no specific suggestions for improvement.

Fadri Gottschalk

Yes, my impression is that the authors took the comments seriously and did a very good job revising the manuscript and responding to the suggestions/comments.

Some remaining suggestions:

Missing current literature: There are still some additional studies on MWCNTs that possibly should be included (please see above comments).

Critique on the comparison with decaBDE: As mentioned above, this comparison needs some additional legitimation, and an introductory explanation from a material property perspective, as to why the comparison of MWCNT to decaBDE is meaningful.

Missing gray literature: I know the report cannot fully present an exhaustive review of all the literature. However, I would tell the reader in more detail how peer review, non-peer review, and gray literature, etc., were treated.

As suggested once, I also think that the authors could possibly add a final concluding chapter or remarks by giving some prudent statements on risk assessment that go beyond the modest purpose of identifying and prioritizing research gaps.

Stig I. Olsen

I find that the comments and responses have been thoroughly described in Appendix I. I particularly like that the comments and responses have been grouped and thus provide a better overview of how the EPA has responded to the comment. This makes it more transparent and clear.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

Charge Question 8
In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

Karin Aschberger

Yes, comments were either addressed in the document or justifications were given where not. The reader friendliness has improved by focusing on MWCNTs and moving DecaBDE to an Annex. While it is appreciated that the main document makes reference to the Annex, references from the Annex to the main document should be avoided, as it makes it quite confusing to read.

Jaclyn Cañas-Carrell

It is evident that EPA was highly responsive to input from comments. Here are a few things that stood out regarding EPA responsiveness to comments:

- Some reviewers did not see the utility of comparisons to decaBDE, while others did see the utility of the comparison. As a result, EPA moved the majority of the text related to decaBDE to an Appendix and then inserted text boxes on how decaBDE data might inform future research for MWCNTs.

- Based on the comments, it seems that the External Draft was not as concise and focused as this revised version. I found the revised version to be very easy to follow and the use of text boxes and movement of most of the text related to decaBDE to an Appendix allowed this version to seem more focused and important ideas or research priorities really stood out.

- EPA also seemed to be very responsive to comments related to the literature (or lack thereof) used in the document. In fact, suggestions from reviewers led to the inclusion of the Additional Information Highlight Boxes which really added to the document.

P. Lee Ferguson

Comparison of the case study document in its present form to the draft for external review, together with a careful read of the stakeholder comments, indicates that EPA was very responsive to input. It is evident that each particular comment was addressed and I have found many cases in which the document was changed accordingly. The two most significant changes made were to relocate the bulk of the DecaBDE discussion to an appendix and the incorporation of informational and comparative "text boxes" in the main document to highlight priority areas and identify areas in which relevant comparisons could be made between MWCNT and DecaBDE properties and behavior. I believe that these were appropriate and very useful changes that have improved the document considerably. The only exception is that I do not agree fully

with the EPA's approach in "Response Category 2", wherein new information or references brought to light during the external review were added as separate, highlighted (in blue) information text boxes. I believe that the new references and/or information should have been more seamlessly integrated with the existing main text body. There may be cases where the information would have been best presented in such "call-outs", but I would estimate that such cases would be the exception rather than the rule, so most newly identified literature should have been added directly to the text. I will qualify this statement by saying that it was somewhat difficult for me to track all of these additions from comment to response to information box, so I'm unable to identify specific areas where this could be corrected.

Fadri Gottschalk

Please see comments on Questions 6 and 7.

Stig I. Olsen

It is evident that EPA has been responsive to the comments.

Potential Utility of Knowledge Maps

Charge Question 9
Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

Karin Aschberger

In principle, the rationale is clear and gives a very nice overview. Some steps are not 100% comprehensible (e.g. purple colour for potential value):

- Figure J-2: I suggest to put lipophilicity together with water solubility as they are usually antipods. Lipophilicity would then also influence dispersion (add arrow). The arrow from bioaccumulation should not just go to plants, but to biota as it could also impact terrestrial animals (earthworms); an additional arrow should go to aquatic biota.

- Figure J-3 and J-4: It is interesting to notice that for DecaBDE all movements are known, but there are no strong movements, whereas for MWCNTs there is only one known movement which is considered strong. Is evidence not sufficient to consider sediment as a known sink?

- Figure J-6: The differences between the different MWCNT types are not clear and should be better explained. Circle and Octagon are both MWCNT – if it is the same, why not use the same symbol. If different, please explain. Bundled MWCNT – only by sorption?

Jaclyn Cañas-Carrell

Not being familiar with Knowledge Maps, I have no real context for comparison. However, the pilot project was clearly described and easy to understand. After reading the text, it was easy to interpret the maps. I did not find anything that needs further clarification. The maps appear to concisely present data discussed in Chapter 3 and Appendix D.

P. Lee Ferguson

I do believe that the rationale for the pilot project is well-described. I have no problems with that aspect of Appendix J. My more substantive comments are detailed below.

Fadri Gottschalk

Yes, absolutely. However, at the end of the appendix, I'd like to see some discussion or conclusion concerning the objective of this subproject that was to develop methods (for visually and concisely presenting information) in CEA.

Stig I. Olsen

The rationale is OK as described. I find that the knowledge maps provide very good visual information. I must admit that the text in itself didn't provide a good understanding of the structures of the figures with nodes and edges until I saw the figures (but maybe that's my English that does not suffice). Furthermore, the text (and maybe the figures as well?) lacks good explanation of what is the "weight of evidence" for the information conveyed regarding the l Physicochemical Properties Map (PPM). There is a mix-up between 'varying parameters' and 'unknowns' in my understanding. And the purple "potential," does that represent lack of evidence or what? How is it represented that there is no knowledge?

Potential Utility of Knowledge Maps

Charge Question 10
As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

Karin Aschberger

The Maps – with the dotted line – in principle help to identify knowledge gaps. However, for MWCNTs, almost all lines are dotted so is there a knowledge gap in general? Maybe you could differentiate between suspected pathways (something is known) and those where there is no knowledge at all.

Jaclyn Cañas-Carrell

The maps are extremely useful in conjunction with the references in Appendix D (and Chapter 3) to identify potential data gaps to drive future research to assist in risk assessment/management. The maps are easy to follow once one has read the explanation of how to read and interpret the maps. These maps are extremely valuable, especially for those conducting research with MWCNTs.

P. Lee Ferguson

Overall, I think that the knowledge maps are useful for conveying general processes and properties of MWCNT and DecaBDE relevant to the CEA as implemented. However, I believe that these would be MUCH more useful if the modules and connectors were made more quantitative. It should be possible to estimate (from literature) magnitudes of rates, concentrations, and volumes relevant to the processes of transport, transformation, and physicochemical apportioning in the environment for BOTH the MWCNT and DecaBDEs. This would make the comparisons between the two candidate flame retardant materials much more robust. Also, if they are to be used, these knowledge maps should be placed in Chapter 3.

Fadri Gottschalk

Yes, if the model input data classification (known, not available, and similar descriptions) is used for all maps and if this classification reflects the newest evidence available. If not, this leads to misleading conclusions and non-legitimate decisions in this context.

Stig I. Olsen

I think that the TfM and TpM clearly illustrate the limited knowledge on MWCNT environmental fate. The same clarity is missing in the PPM. I don't have good ideas for how to improve this.

Potential Utility of Knowledge Maps

Charge Question 11
Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

Karin Aschberger

I didn't have time to read this chapter in detail – there is not much text there – but it seems that the most important issues are captured. I would suggest moving the maps to Chapter 3 so that there can be a direct link/comparison. Otherwise, the maps are isolated without explanation (see comment above).

Jaclyn Cañas-Carrell

Yes, each of the maps (PPM, TpM, and TfM) accurately and clearly presented the information presented both in Chapter 3 and Appendix D. In fact, the Knowledge Maps helped to concisely present the information presented. See answers to Q9 and Q10 above as further support of this answer.

P. Lee Ferguson

The three classes of knowledge maps do a reasonable job of summarizing (visualizing) the connections among processes and the overall information conveyed in the case study, but again – they should be made quantitative if they are to be of much use. Also, in Figure J-2, "water solubility" with or without surfactants is not an appropriate term for MWCNT. A more accurate term would be dispersibility.

Fadri Gottschalk

Basically, yes. These maps are based on Table 3-1 and Table H-3 and transform information in tabular form into figures, like flow charts. Figure J-2 reflects Table H-3; however, this table is based on old and more non-quantitative data for MWCNTs—there is newer (partially contradicting) evidence available, as listed above. I would adapt this figure by considering these data or at least, for example, the modeling studies on MWCNT and environment that the authors referred to in Table 3-2. The same applies to Map J-4.

Terrestrial box: Is a distinction of natural, agricultural, and urban soils meaningful/feasible?

I know the figures already contain a legend; however, I think that a clear map description directly appended to the table would facilitate analysis and understanding.

Stig I. Olsen

Figure J-2 seems to lack potential coating/functionalization and the consequences of this. But apart from this, I believe they do summarize the information given in other parts of the document.

VI. INDIVIDUAL REVIEWER COMMENTS

Review By:
Karin Aschberger, Ph.D.

Peer Review Comments on EPA's Draft Document
Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

Karin Aschberger, Ph.D.
European Commission - Joint Research Centre
Ispra, Italy

I. GENERAL IMPRESSIONS

The document provides a comprehensive overview on the use of MWCNTs as flame retardants in textiles. It covers important issues such as life cycle, transport/fate, exposure, and hazard, and gives recommendations for identifying and prioritizing research needs. The document is very clear and interesting to read.

According to the title, a comparison to DecaBDE flame retardant coatings should be made. This relates more to the previous version (July 2012 for public consultation) of the document, where MWCNT was set in direct comparison to Deca BDE. In the current document, most of the content on Deca BDE was moved to an Annex, which is appreciated as the document focuses more on MWCNTs; however, a change in the title could be envisaged to better fit the current scope.

I am not completely sure how much DecaBDE contributes to inform MWCNT assessments in relation to the research priorities, as these are very different compounds with different characteristics and behaviour in the environment and in the human body. In my review, the comparison should relate more to the (expected) risks and MWCNT could be used as an alternative to the phased out DecaBDE. For this, a general overview with comparisons could be presented.

In addition, MWCNT cannot be used alone in textiles (and other applications) as flame retardants because they do not comply with the flammability test and instead are used with other flame retardants to decrease the flammability synergistically. Therefore, in my view, it is not adequate to directly compare MWCNT alone with DecaBDE. A representative compound which is used in combination with CNTs (e.g., phosphonates) should be included in the comparison.

Additional Information:

- Just a remark. 'Comprehensive Environmental Risk Assessment' – as a European, I was wondering about the 'Environmental' as we usually speak about ' Human Health and Environmental' and would not consider Human Health to be included in an Environmental Risk Assessment.

- Our group is currently taking part in the FP7 Project 'DEROCA' *Development of safe and eco-friendly flame retardant materials based on CNT co-additives for commodity polymers.* Our task is a comparative risk assessment to other flame retardant solutions. If you are interested (we have just started and no results yet available), here is the website

link: http://www.deroca.eu/DEROCA_WEB/UK/Home.awp

II. RESPONSE TO CHARGE QUESTIONS

Completeness and Accuracy

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

The science is, in general, accurately and clearly conveyed throughout the document.

I consider that the data discussed in this document have been retrieved from the latest peer-reviewed scientific papers and most accurate reviews. However, there are some specific areas and references that can be extended and included.

References (often not the original references, but those of reviews. I can only refer to those that I know very well):

- Table 1-8: ECB 2003: EU Risk Assessment Report as reference for DecaBDE phys-chem properties; and

- Table 1-9: Johnston and Aschberger as references for MWCNT phys-chem properties. Please refer to original sources, where these properties have been determined.

Be consistent with references. For example, in Text Boxes 5-1 (but also others), only part of the text is referenced. Either give references for all statements or no references in text boxes and only in the accompanying text.

Additional relevant information sources on MWCNTs could be considered:

- There is a REACH registration dossier on MWCNT (for Baytubes and Nanocyl), parts of which are publicly available. It contains, for example, information on TG GLP studies which were not published in peer-reviewed papers. This information could be used to fill gaps in Table 5-1 and the corresponding text. Link: http://apps.echa.europa.eu/registered/data/dossiers/DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031/DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031_DISS-b281d1a0-c6d8-5dcf-e044-00144f67d031.html

  It also gives rough information on manufacturing volume, as they were registered for the tonnage volume: 100-1000 tons/year.

- The Japanese Risk Assessment of Manufactures Nanomaterials – CNT (NEDO project): Nakanishi, J., Ed. Risk assessment of manufaucured nanomaterials: Carbon nanotube (CNT). Final report issued on August 12, 2011. NEDO project (P06041) Research and development of nanoparticle characterization methods. Link:

http://www.aist-riss.jp/main/modules/product/nano_rad.html?ml_lang=en

- Human Health Hazard Assessment and Classification of Carbon Nanotubes. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Safe Work Australia. October 2012. ISBN 978 0 642 78542 8 [Online PDF]. Link: http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/human-health-hazard-assessment-and-classification-of-carbon-nanotubes

I disagree with the following statements in Chapter 5:

5-10: Subchronic – chronic systemic toxicity

The way it is presented it seems that there are no subchronic/chronic studies (by any route) available – or no studies testing systemic effects. (In vivo) - Studies are not made separately for local or systemic effects, but they can be observed and/or reported. There are two subchronic inhalation studies with MWCNTs available which have not reported systemic effects. In addition, the Pauluhn study included a 6 M post-exposure observation period – this could be added where the study is described.

5-14: Relevance of in vitro data

The introductory sentence should be revised.

There is a general requirement to replace animal studies by alternative methods and some in vitro test are validated and regularly used in regulatory risk assessment: mutagenicity (usually only in vivo confirmation of positive in vitro results), dermal absorption, and skin and eye irritation. A good overview on the suitability of in vitro methods (not validated for NM yet) for NM hazard assessment are given in:

- SCCS 2012: Guidance on the safety assessment of nanomaterials in cosmetics. Link: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_005.pdf

- Hartung et al. 2011. Alternative in vitro assays in nanomaterial toxicology. Link: http://onlinelibrary.wiley.com/doi/10.1002/wnan.153/abstract;jsessionid=DF763EC777E464BDF520FF2C46822C6C.d03t03

Several EU framework projects are focusing on development of alternative methods for NM toxicity testing, in vitro-in vivo extrapolation (e.g., ITS-Nano, MARINA, ENPRA).

Further information on in vitro data and alternative methods to support toxicological studies can be found in:

- Adler, S., D. Basketter, et al. (2011). Alternative (non-animal) methods for cosmetics testing: current status and future prospects-2010. Archives of toxicology 85(5): 367-485.

- Hartung, T., B. J. Blaauboer, et al. (2011). An expert consortium review of the EC-

commissioned report "alternative (Non-Animal) methods for cosmetics testing: current status and future prospects - 2010". ALTEX 28(3): 183-209.

Clarity and use of priority areas to support research planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

Priority areas can be clearly identified as they are clearly highlighted throughout the document. The presentation of the division of importance and confidence ranking (and associated colours) is considered useful, especially the confidence because it plays an important role in the regulatory decision making. For example, in Chapter 4, Section 4.2 Human Exposure and Kinetics Leading to Dose, priority research areas identified inhalation exposure route as the highest priority area, followed by ingestion and dermal exposure. This information is supported by the literature presented.

In each subsection, exposure scenarios sorted by exposure route (inhalation, oral, and dermal) are presented for the occupational scenarios. For clarity, a summary table of this information highlighting the activities related to each kind of exposure with exposure levels data (if available) is suggested for:

- Synthesis, Processing, and Handling.
- Formulation of Flame Retardant, Application to Textiles, Upholstering.
- Storage of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products.
- Disposal and Recycling of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products.

Additional Comments:

- The identified priority areas for Human Health are in accordance with our findings within the ENRHES (http://ihcp.jrc.ec.europa.eu/whats-new/enhres-final-report) and the currently running ITS-Nano FP7 project (http://www.its-nano.eu/). For the Environment, there is a different view on the terrestrial compartment. It was identified as priority research area under ENRHES and ITS-Nano. Sediment and soil are usually sinks for NM (e.g., see our paper: Aschberger. Environment International 37 (2011) 1143–1156). Sedimented NM in wastewater, which was also identified as priority, could end up in soil

together with sludge.

- In general, reasons for not prioritized areas could be better explained (e.g., terrestrial environment).

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

Please find some additional references below and in the Specific Observations section (not exhaustive, as I didn't have time to check everything carefully):

Studies on release of polymer bound CNTs (it seems that not much information has been included in the report):

- Wohlleben et al. 2011. On the lifecycle of nanocomposites: comparing release fragments and their in vivo hazards from three release mechanisms and four nanocomposites. Small. No 16, 2384-2395.

- Wohlleben et al. 2013. Elastic CNT-polyurethane nanocomposite: synthesis, performance and assessment of fragments released during use. Nanoscale 369-380

- Stahlmecke et al. (IUTA Duisburg Germany) 2013. Investigations on the possible CNT release at the end-of-Life of CNT-composites. Poster (not found on internet, but could be made available to you).

- Ogura et al. (AIST, TASC Japan) 2012. Potential release of carbon nanotubes from their composites during grinding. Poster at nanosafe 2012: http://www.certh.gr/dat/A974408A/file.pdf

- Movahedi, Alireza 2008. Risk assessment of nanoparticle release from the structure of polymeric nanocomposites – Master Thesis University Goteburg: http://libris.kb.se/bib/12060839

Environmental Fate:

- O'Carroll, D. M., Liu, X., Mattison, N. T., Petersen, E. J. 2013. Impact of size on carbon nanotube transport in natural porous media. *Journal of Colloid & Interface Science*, 390(1), 96-104.
- Zhang, L., Petersen, E. J., Zhang, W., Chen, Y. S., Cabrera, M., Huang, Q. 2012. Phase distribution of 14C-labeled multi-walled carbon nanotubes in aqueous systems containing model solids: clay. *Environmental Pollution*. 166, 75-81.

- Liu, X., O'Carroll, D.M., Petersen, E.J., Huang, Q., Anderson, L. 2009. Mobility of multi-walled carbon nanotubes in porous media. Environmental Science & Technology. 43, (21), 8153-8158.

Ecotoxicity:

- Petersen, E. J., Pinto, R. A., Mai, D. J., Landrum, P. F., Weber, W. J., Jr. 2011. Influence of Polyethyleneimine Graftings of Carbon Nanotubes on their Accumulation and Elimination by and Toxicity to *Daphnia magna*. *Environmental Science and Technology*. 44, (3), 1133-1138.

- Galloway, Tamara, et al. "Sublethal toxicity of nano-titanium dioxide and carbon nanotubes in a sediment dwelling marine polychaetes." *Environmental Pollution* 158.5 (2010): 1748-1755. **(NB! SWCNT & marine sediment!!!). NOEC > 0.03 g/kg to** *A*renicola marina (lugworm)

Bioaccumulation:

- Petersen, E. J., Pinto, R. A., Mai, D. J., Landrum, P. F., Weber, W. J., Jr. 2011. Influence of Polyethyleneimine Graftings of Carbon Nanotubes on their Accumulation and Elimination by and Toxicity to *Daphnia magna*. *Environmental Science and Technology*. 44, (3), 1133-1138.

- Petersen, E. J., Akkanen, J., Kukkonen, J. V. K., Weber, W. J., Jr. 2009. Biological Uptake and Depuration of Carbon Nanotubes by *Daphnia magna*. Environmental Science & Technology. 43, (8), 2969-2975.

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

The document is mainly focusing on the research areas but does not include recommendations on how this could be achieved. In addition to increasing the knowledge about MWCNTs or NM in general, there should be also focus on better exploitation of existing data, reading across and the use of alternative methods (in vitro/QSAR).

The consideration of other impacts such as energy, climate change, economics etc., is appreciated. As mentioned above, it should be considered that MWCNT alone will not be sufficient to replace DecaBDE.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

The document organization is logical although sometimes it is repetitive and could be shorter in some parts. The extended executive summary relating to the different chapters gives a clear overview on the content of the document and helps to focus on specific areas.

In my opinion, within Chapter 4, a better separation between human and environmental exposure scenarios and data would be helpful. This separation is achieved in Chapter 5, in which the

information on potential human health and ecological impacts of CNTs are well divided in two subsections (5.1. Human Health Effects and 5.2. Ecological Effects).

Responses to public and peer comments on the MWCNT case study ERD

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

Comments are transparently addressed.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

Comments are transparently and clearly conveyed. The double presentation of original comments and summarized comments make it very transparent.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

Yes, comments were either addressed in the document or justifications were given where not. The reader friendliness has improved by focusing on MWCNTs and moving DecaBDE to an Annex. While it is appreciated that the main document makes reference to the Annex, references from the Annex to the main document should be avoided, as it makes it quite confusing to read.

Potential Utility of Knowledge Maps

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

In principle, the rationale is clear and gives a very nice overview. Some steps are not 100% comprehensible (e.g. purple colour for potential value):

- Figure J-2: I suggest to put lipophilicity together with water solubility as they are usually antipods. Lipophilicity would then also influence dispersion (add arrow). The arrow from bioaccumulation should not just go to plants, but to biota as it could also impact terrestrial animals (earthworms); an additional arrow should go to aquatic biota.

- Figure J-3 and J-4: It is interesting to notice that for DecaBDE all movements are known, but there are no strong movements, whereas for MWCNTs there is only one known movement which is considered strong. Is evidence not sufficient to consider sediment as a known sink?

- Figure J-6: The differences between the different MWCNT types are not clear and should be better explained. Circle and Octagon are both MWCNT – if it is the same, why not use the same symbol. If different, please explain. Bundled MWCNT – only by sorption?

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

The Maps – with the dotted line – in principle help to identify knowledge gaps. However, for MWCNTs, almost all lines are dotted so is there a knowledge gap in general? Maybe you could differentiate between suspected pathways (something is known) and those where there is no knowledge at all.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

I didn't have time to read this chapter in detail – there is not much text there – but it seems that the most important issues are captured. I would suggest moving the maps to Chapter 3 so that there can be a direct link/comparison. Otherwise, the maps are isolated without explanation (see comment above).

III. SPECIFIC OBSERVATIONS

Page	Line # or Paragraph	Comment or Question
4-1	L17	Explain 'abiotic receptors' better.
4-3 Text Box 4.1	4.1.1. Dose and Exposure Metrics	In this section more information on quantification of carbon nanomaterials in vivo could be given. In 2011, a review was published focusing on isotopic labelling and tracing methods. Please see reference: Wang, H., S.-T. Yang, et al. (2012). "Quantification of Carbon Nanomaterials in Vivo." Accounts of Chemical Research 46(3): 750-760.
4-31	Table 4-1. Established inhalation reference values and	According to the review : Morimoto, Y., M. Horie, et al. (2012). "Inhalation Toxicity Assessment of Carbon-Based Nanoparticles." Acc Chem Res.

Page	Line # or Paragraph	Comment or Question
	recommendations applicable to MWCNTs.	This value is 30ug/m3 and was calculated in rats exposed to SWCNTs from two studies. According to the authors, this value also applies to MWCNTs. This result is reported in: Nakanishi, J., Ed. Risk assessment of manufactured nanomaterials: Carbon nanotube (CNT). Final report issued on August 12, 2011. NEDO project (P06041) "Research and development of nanoparticle characterization methods", and the data was calculated from two animal studies: 1. Morimoto, Y., M. Hirohashi, et al. (2012). "Pulmonary toxicity of well-dispersed multi-wall carbon nanotubes following inhalation and intratracheal instillation." Nanotoxicology 6(6): 587-599. 2. Kobayashi, N.; Naya, M.; Mizuno, K.; Yamamoto, K.; Ema, M.; Nakanishi, J. Pulmonary and systemic responses of highly pure and well-dispersed single-wall carbon nanotubes after intratracheal instillation in rats. Inhalation Toxicol. 2011, 23, 814–824.
4-18	Additional Information Highlight Box 11: MWCNT dermal absorption	In vitro data on dermal absorption is provided in this paper: Vankoningsloo, S., J. P. Piret, et al. (2010). "Cytotoxicity of multi-walled carbon nanotubes in three skin cellular models: effects of sonication, dispersive agents and corneous layer of reconstructed epidermis." Nanotoxicology 4(1): 84-97. This reference can be also added in Appendix F in Table F-2.
4-20	4.2.1. Occupational Exposure Pathway Scenarios L20-22	Suggested reference for inhalation study of MWCNT by the wet aerosolization method: Morimoto, Y., M. Hirohashi, et al. (2012). "Pulmonary toxicity of well-dispersed multi-wall carbon nanotubes following inhalation and intratracheal instillation." Nanotoxicology 6(6): 587-599. In the inhalation study, rats were exposed to 0.37 mg/m(3) aerosols of well-dispersed MWCNTs (>70% of MWCNTs were individual fibers) for 4 weeks, and were sacrificed at 3 days, 1 month, and 3 months after the end of exposure. The inhalation exposures delivered less amounts of MWCNTs into the lungs, and therefore less pulmonary inflammation responses was observed, as compared to intratracheal instillation. The results of this study show that well-dispersed MWCNT can produce pulmonary lesions, including inflammation.
I-5	Table I.3	For clarity Table I-3 could be moved previous to the introduction to I.1.2. Appendix Organization. (In page I-4, after line 8)
I-5	Table I.3	Response category 1; Actions Taken: Moved unprioritized sections to Appendix.

Page	Line # or Paragraph	Comment or Question
		To comply with this action, box of unprioritized research area in page 4-2 to Appendix.
5-5	Table 5-1	Please note that an acute dermal (TG 402 GLP) study is available from the REACH registration dossier Add references to all X where there are results (see link above)
5-7	7-9	Add Shvedova 2008: Am J Physiol Lung Cell Mol Physiol 295:L552-565 as reference for SWCNT inflammatory effects – currently you only list MWCNT authors.
5-7, 5-9 – 5-10	Systemic Toxicity	5-7: Line 17 .. although no subchronic inhalation studies were identified for systemic toxicity … The way it is presented it seems that there are no subchronic/chronic studies (by any route) available (see also table 5-1). – the fact is that no systemic effects were observed/described from available studies. Subchronic: 2 Inhalation studies (Pauluhn, Ma-Hock), Chronic (injection): Sakamoto 2009 (52 W), Muller 2009 (2y); Add Muller 2009 and Poland 2008 study on page 5-7 where you describe that certain type of MWCNTs could behave in a manner similar to asbestos – as Muller/Poland showed that short MWCNTs did not induce mesotheliomas.
5-9	1-14 13-14	Health Reference Values: suggest to add reference to Table 4-1 which is more comprehensive and includes more values (e.g. the Pauluhn and NEDO value). I did not find a description of how the Aschberger values where derived in 5.1.3. Maybe delete this.
5-13	L17	Footnote 16: not clear what is meant to express: not relevant for MWCNT or for inhalation exposure? – only the first sounds logic
5-17	L14-15	These studies are not a proof for lung carcinogenicity – but rather a proof that if they reach a tissue from where they cannot easily be removed (mesothelium) they can be carcinogenic. The main concern raised by these studies is that if MWCNT would reach the mesothelium they would act like asbestos. In the lung there would be clearance and the reaction could be different. The risk of lung carcinogenicity is probably similar to other NP. Therefore I suggest to rephrase; you could say: 'Another target organ of MWCNT could be the lung' (but there is no study yet showing that).
5-17	5.1.11 Carcinogenicity	You could write certain types of CNTs (long rigid) induced mesotheliomas, with certain diameter … – see text in 6-34 which I suggest to move to Chapter 5. In addition: Nagai, H., Y. Okazaki, et al. (2011). "Diameter and rigidity of multiwalled carbon nanotubes are critical factors in mesothelial

Page	Line # or Paragraph	Comment or Question
		injury and carcinogenesis." Proceedings of the National Academy of Sciences of the United States of America 108(49): E1330-1338. In the section 5.1.11 on Carcinogenicity, I suggest you reference a paper from 2011 in which a relationship between diameter and rigidity of MWCNT as key factor in mesothelial injury and cancinogenesis. The authors tested the potential carcinogenesis of different MWCNT after i.p. injection into rats. Higher frequency of malignant mesothelioma was observed when animals were treated CNT with higher diameter and length. Carcinogenicity was independent of fibre suspension characteristics as CNT samples contained same number of dispersed fibres and lacked agglomerates. Specific genetic alterations associated with mesotheliomas are reported in this study.
5-17	L20	Disagree that results from intratracheal instillation studies are qualitatively similar to inhalation studies. Due to the bolus effect the clearance in the lung is overwhelmed – therefore not only quantitatively but also qualitatively different effects (Ref: Oberdoester 2010, J Intern Med 267: 89-105). See also Morimoto 2012 study as listed above.
F-13 – F-17	Table F5-F6	Inhalation studies: suggest not to list intratracheal instillation (+ intranasal injection) studies as 'inhalation' – maybe use: 'pulmonary exposure'
6-34	6.3.4 Impacts	6.4.3.1, 6.3.4.2; It seems that in this part newer results are presented than in Chapter 5 – should this not be moved there? For example, page 5.17
6-35	18	You cannot identify a NOEL or LOEL for consumers – you can only determine a reference value (which considers different assessment factors) – please rephrase
E-11	Table E-6	Is there only data for occupational air and no data for environmental compartments as for Deca-BDE?

Review By:
Jaclyn Cañas-Carrell, Ph.D.

Peer Review Comments on EPA's Draft Document
Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

Jaclyn Cañas-Carrell, Ph.D.
Texas Tech University
Lubbock, TX, USA

March 26, 2013

I. GENERAL IMPRESSIONS

Overall, the case study document is very well written, organized, and very informative. It is a bit strange that the case study is so focused on one type of application of MWCNTs, especially one that is not the most common application and one that may never become a major application of MWCNTs. However, the majority of the information and Priority Research Areas included in the document provides guidance for general research needs for MWCNTs, independent of the application. Therefore, this document will be of use to CNT and MWCNT researchers even if these nanomaterials are not widely used in flame-retardant textile coatings.

The presentation of the literature and the identified Priority Research Areas was clear and informative to drive future research directions to ultimately support risk assessment and management of MWCNTs.

With regards to presentation of the document, it is well organized and presented in a very logical manner. The introductory chapter does an excellent job at setting the stage for the remainder of the document as well as providing a context for why decaBDE is included in the document. The extensive use of headings and subheadings is very useful to the reader. The use of various text boxes highlighting important information and identifying Priority Research Areas really allowed for the most important information to be clearly stated and stand out to the reader. Overall, the document is easy to read and is presented in a clear and logical manner.

II. RESPONSE TO CHARGE QUESTIONS

Completeness and Accuracy

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

To the best of my knowledge, I believe the science is accurately conveyed throughout the document. No revisions are needed. The extensive review of the science and document that preceded this current review has resulted in a well written and accurate version of the final document.

Clarity and Use of Priority Areas to Support Research Planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

Yes, the Priority Research Areas are clearly identified throughout the document. Putting the Priority Research Areas in text boxes really highlights the priority areas. In addition, the discussion of each Priority Research Area in Chapter 6 helps to further emphasize the areas and provides an overall succinct summary of the research needs related to MWCNTs in flame-retardants.

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

There are two additional studies that could be considered for inclusion to support the Priority Research Areas:

3. Irin et al. (2012) is listed in Highlight Box 10 but not listed in the tables in Appendix B.

    a. Irin, F, B Shrestha, JE Cañas, M Saed and MJ Green. 2012. Detection of carbon nanotubes in plant roots through microwave-induced heating. Carbon 50:4441-4449.

4. Li et al. (2013) could be added to pp. 6-24, line 30. This paper demonstrated no substantial uptake of MWCNTs in earthworms in soil.

    a. Li, S, F Irin, FO Atore, MJ Green, and JE Cañas-Carrell. 2013. Determination of carbon nanotube bioaccumulation in earthworms measured by a microwave-based detection technique. Science of the Total Environment, In press. doi: 10.1016/j.scitotenv.2012.12.037.

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

The document definitely supports research planning to inform future risk assessments. The questions outlined at the end of the green text boxes (DecaBDE Can Inform MWCNT

Assessment) are very helpful to outline research needs. In addition, the Priority Research Area text boxes (and Unprioritized Research Areas) also helped to outline research needs. Chapter 6 is also instrumental in providing further discussion to inform research planning.

With the exception of the Impacts Priority Research Area for Aquatic Biota (p. 5-19), the other text boxes clearly define research gaps and questions to ask. After reading Chapter 6.3.4.3, particular research needs are more apparent. This particular text box could be improved to include what is discussed in Chapter 6.3.4.3.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

The organization of the document is excellent. It flows in a logical manner and is easy to understand, at least to someone with a toxicology background and that does nanotoxicology research. While I cannot speak from the perspective of someone with less background, I believe the document does a good job in defining key concepts or ideas for those perhaps not as versed in toxicology or nanotoxicology.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

Yes, peer and public stakeholder comments are clearly summarized and conveyed through the use of tables. After looking at Tables I-12 through I-14, it appears that comments are clearly summarized in Tables I-4 through I-9 and I-11. No further revisions are necessary.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

Yes, EPA responses to comments are also transparently and clearly conveyed through the use of tables. EPA responses are detailed with specific sections, Priority Research Area Boxes, or Highlight Text Boxes where revisions were incorporated as suggested. In addition, EPA responses were fully justified in the few cases where no change was made.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

It is evident that EPA was highly responsive to input from comments. Here are a few things that stood out regarding EPA responsiveness to comments:

- Some reviewers did not see the utility of comparisons to decaBDE, while others did see the utility of the comparison. As a result, EPA moved the majority of the text related to decaBDE to an Appendix and then inserted text boxes on how decaBDE data might inform future research for MWCNTs.

- Based on the comments, it seems that the External Draft was not as concise and focused as this revised version. I found the revised version to be very easy to follow and the use of text boxes and movement of most of the text related to decaBDE to an Appendix allowed this version to seem more focused and important ideas or research priorities really stood out.

- EPA also seemed to be very responsive to comments related to the literature (or lack thereof) used in the document. In fact, suggestions from reviewers led to the inclusion of the Additional Information Highlight Boxes which really added to the document.

Potential Utility of Knowledge Maps

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

Not being familiar with Knowledge Maps, I have no real context for comparison. However, the pilot project was clearly described and easy to understand. After reading the text, it was easy to interpret the maps. I did not find anything that needs further clarification. The maps appear to concisely present data discussed in Chapter 3 and Appendix D.

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

The maps are extremely useful in conjunction with the references in Appendix D (and Chapter 3) to identify potential data gaps to drive future research to assist in risk assessment/management. The maps are easy to follow once one has read the explanation of how to read and interpret the maps. These maps are extremely valuable, especially for those conducting research with MWCNTs.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

Yes, each of the maps (PPM, TpM, and TfM) accurately and clearly presented the information presented both in Chapter 3 and Appendix D. In fact, the Knowledge Maps helped to concisely present the information presented. See answers to Q9 and Q10 above as further support of this answer.

III. SPECIFIC OBSERVATIONS

Page	Line # or Paragraph	Comment or Question
2-7	Green Text Box	It is awkward that Table 2-3 is mentioned before Table 2-1 and 2-2.
2-9	4-5	CNTs deposits should probably just be CNT deposits.
2-20	Priority Research Area Text Box	The first sentence states that 9 out of 13 RTI workshop participants identified the MATERIAL PROCESSING STAGE of the MWCNT…However, the figure indicates that 9/13 participants found USE; material processing is not mentioned and this figure is found under the Heading 2.4 Use. I believe the first statement must have been cut and paste from elsewhere.
4-3	Neutral Research Area Text Box	It seems the heading for the Neutral Research Area is incorrect as it says – Neutral Research Area: Environmental Transport, Transformation and Fate, which is the same title for the Neutral Research Area in Chapter 3. I'm not sure what the title heading should be.
4-23	Priority Area: Exposure Route Text Box	This research area pertains to consumer exposure and yet the 2nd sentence says that the 9 participants were asked to rate the importance of ingestion, inhalation and dermal OCCUPATIONAL exposures. It should be CONSUMER exposures.
6-31	Line 9	Should be "as noted above" instead of "as note above."

Review By:
P. Lee Ferguson, Ph.D.

Peer Review Comments on EPA's Draft Document *Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles*

P. Lee Ferguson, Ph.D.
Duke University
Durham, NC

I. GENERAL IMPRESSIONS

My overall impression of this case study is that it was carefully, thoughtfully, and accurately drafted. After careful review, it is clear that the presentation benefited greatly from the comments of the external reviewers. In particular, the comparative aspect of this case study was quite interesting. While DecaBDE and MWCNT share little in the way of physicochemical properties, their comparison from a use-to-exposure life cycle perspective adds value to the case study. I believe that this is particularly true in the case of MWCNT, for which very few real measures of exposure and/or environmental occurrence have been made (in contrast to DecaBDE). However, inclusion of detailed direct comparison between these materials within the main body of the CEA document would have been unnecessarily tedious and distracting from the primary goal of the case study. The decision to move most of the DecaBDE-relevant information to the appendix was well-founded, and the inclusion of comparative "text boxes" within the main text body are useful. I am unsure that MWCNTs will ever find widespread use in flame retardant application (this is still a niche use with only one example and a few literature citations), so the focus on this particular incarnation of MWCNT use is dubious. I find that the research priority areas for MWCNT identified during the prioritization process are indeed very important and relevant, but there is some inconsistency. In particular: "ecological impacts of MWCNT in aquatic biota" was identified as a priority area, but both exposure and dose of MWCNT in ecological populations were not identified as priority. These aspects of MWCNT behavior are intimately linked and it seems inappropriate to separate their priorities.

II. RESPONSE TO CHARGE QUESTIONS

<u>Completeness and accuracy</u>

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

In general, I have found that the authors and the external reviewers have done an admirable job of summarizing the latest research findings concerning the state of the science regarding MWCNT fate, exposure, and effects. In particular, while there is broad consensus for certain properties and behaviors of MWCNTs in the environment (e.g., their tendency to aggregate and to associate with particulates in aqueous systems), others are more controversial (e.g., potential for bioaccumulation or ability to cross cell membranes). These areas of respective clarity or lack thereof are very important to identify in a case study describing materials for which fate/transport models based on physicochemical properties are of limited relevance. I believe that this aspect

was well described in the case study. I do feel that the entire case study suffers from a relatively narrow focus on MWCNT. In many cases, SWCNT may behave in a very similar fashion to MWCNT in environmental and biological systems, and I feel that the case study would have benefited from inclusion of the relevant research (e.g. fate and transport, analytical methods, exposure predictions) related to SWCNT also. As noted in the document, SWCNT may also be used in textile applications and will therefore experience many of the same routes-of-entry to the environment. Risk assessment of the (likely) more plentiful MWCNT may be informed by research that is relevant to BOTH classes of CNT, including the (likely) lower production-volume SWCNT.

Clarity and use of priority areas to support research planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

The priority areas are very clearly indicated in the document, starting with Figure 1-3 and continuing with highlighted boxes within the main body of the text. In particular, I find the "color-coding" of the boxes within the document easy to follow and helpful.

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

After carefully reviewing the list of references, the descriptions of previous studies and their conclusions, and performing independent literature searches, I believe that the case study has accurately represented the most relevant research findings that can provide guidance for future research supporting risk management of MWCNT. I do not know of any MWCNT-specific studies that have been omitted from the case study. However, as I note above, I believe that the authors and external reviewers missed an opportunity by explicitly excluding environmental fate, transport, and effects data for SWCNT (especially with regard to aquatic fate and mechanisms of human/aquatic toxicity). SWCNT may be expected to behave in very similar ways to MWCNT in the environment (based on similarity of their physicochemical properties) and thus a more complete CEA might have been conducted on "CNT in textiles", irrespective of their intended function in the textile (e.g., flame-retardant vs. stain repellent). In fact, this approach would be quite defensible in light of the fact (as indicated in the box on page 1-28) that MWCNT use as flame retardant coatings in textiles is not yet widespread and is not anticipated to increase dramatically in the future.

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

With the exception of some discontinuities in research priorities (e.g., the identification of "ecological impacts of MWCNT in aquatic biota" as a priority area, while classifying both exposure and dose of MWCNT in ecological populations as lower priority), I found that the document was generally very well structured to guide future research in the area of environmental and health implications of MWCNT. One admirable aspect of this case study is that the environmental and (especially aquatic) exposure/transport/effects characteristics discussed for MWCNT in Chapters 3-5 are relevant for more than just the potential release from use in flame-retardants on textiles. Therefore, the predictions, prioritization, and implications will be valid for MWCNT releases to the environment under a variety of scenarios. Conversely, I find that the weakest part of the document is Chapter 2 (Product Life Cycle), since much of it is focused exclusively on the use of MWCNT in the very narrow application of flame retardants in textiles.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

I've reviewed both the Draft for External Review and the current (revised) Case Study, and I find that the use of information boxes, DecaBDE/MWCNT-comparison boxes, and priority-area boxes throughout the text has greatly improved the logical flow of the document. I do, however, believe that Section 1.1 is unnecessarily verbose and might be better suited to an appendix. Also, Appendix J (Knowledge Maps) – if used at all – would be much more effective as part of the main body of text, perhaps in Chapter 6.

<u>Responses to public and peer comments on the MWCNT case study ERD</u>

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

Yes – I have almost no comments on this aspect of the case study. Appendix I is somewhat difficult to follow, but it is well-organized and cross-referenced among reviewer comments, agency responses, and document edits/amendments. In general, the revisions were made in a very thoughtful and systematic manner.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

As above – yes, the responses to comments are also very well-described in Appendix I. I have no specific suggestions for improvement.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

Comparison of the case study document in its present form to the draft for external review, together with a careful read of the stakeholder comments, indicates that EPA was very responsive to input. It is evident that each particular comment was addressed and I have found many cases in which the document was changed accordingly. The two most significant changes made were to relocate the bulk of the DecaBDE discussion to an appendix and the incorporation of informational and comparative "text boxes" in the main document to highlight priority areas and identify areas in which relevant comparisons could be made between MWCNT and DecaBDE properties and behavior. I believe that these were appropriate and very useful changes that have improved the document considerably. The only exception is that I do not agree fully with the EPA's approach in "Response Category 2", wherein new information or references brought to light during the external review were added as separate, highlighted (in blue) information text boxes. I believe that the new references and/or information should have been more seamlessly integrated with the existing main text body. There may be cases where the information would have been best presented in such "call-outs", but I would estimate that such cases would be the exception rather than the rule, so most newly identified literature should have been added directly to the text. I will qualify this statement by saying that it was somewhat difficult for me to track all of these additions from comment to response to information box, so I'm unable to identify specific areas where this could be corrected.

<u>Potential Utility of Knowledge Maps</u>

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

I do believe that the rationale for the pilot project is well-described. I have no problems with that aspect of Appendix J. My more substantive comments are detailed below.

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

Overall, I think that the knowledge maps are useful for conveying general processes and properties of MWCNT and DecaBDE relevant to the CEA as implemented. However, I believe that these would be MUCH more useful if the modules and connectors were made more quantitative. It should be possible to estimate (from literature) magnitudes of rates,

concentrations, and volumes relevant to the processes of transport, transformation, and physicochemical apportioning in the environment for BOTH the MWCNT and DecaBDEs. This would make the comparisons between the two candidate flame retardant materials much more robust. Also, if they are to be used, these knowledge maps should be placed in Chapter 3.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

The three classes of knowledge maps do a reasonable job of summarizing (visualizing) the connections among processes and the overall information conveyed in the case study, but again – they should be made quantitative if they are to be of much use. Also, in Figure J-2, "water solubility" with or without surfactants is not an appropriate term for MWCNT. A more accurate term would be dispersibility.

III. SPECIFIC OBSERVATIONS

Page	Line # or Paragraph	Comment or Question
1-22	Table 1-5	There should be an entry in this table for MWCNT illustrating mechanism of flame retardancy.
1-27	Table 1-9	Several inconsistencies or errors of usage appear in this table. First – it is misleading to state the purity of MWCNT as "usually > 90%". This is much more variable (shown many times in the literature). I suggest a broader and more defensible range be presented. Also, Chirality is truly meaningless for MWCNT - these properties apply only to individual "layers" of the CNTs or to SWCNT specifically. Finally, citations of "Sigma-Aldrich (2012)" for melting-point, density, etc. are inappropriate. Peer-reviewed literature should be cited for these parameters, not product data-sheets.
2-2 – 2-3	Figure 2-1 and discussion	Based on the known behavior of MWCNT in nearly all media, it is very unlikely that any scenario would result in release of truly "free" MWCNT to the environment. These materials will most likely always exist in homo- or heteroaggregate form. Also, based on information in "Additional Information Box 3", I would consider that release of MIXED chemical/MWCNT flame retardant materials from textiles would be of great concern! This is not mentioned in this section but should be addressed.
2-30	Information Box 5	A reference is quoted stating that most CNTs in wastewater come from tailoring, finishing, use, and degradation of textiles. This is completely speculative and there is no direct evidence of this from analytical studies (even occurrence in wastewater of CNTs is not well-founded based on solid analytical data). This statement should be removed.

Page	Line # or Paragraph	Comment or Question
Chapter 2	Tables comparing MWCNT to DecaBDE	I find these tables very uninformative. They are quite qualitative and in some cases are completely speculative. The overall impression given to the reader is that nearly all processes that apply to release of DecaBDE from textiles may also apply to MWCNT. While this might be true in some cases, I believe that many of the scenarios and processes highlighted in these comparative tables are far too simplistic. There are many physicochemical differences between MWCNT and DecaBDE that would cause behavior in these release processes to differ QUANTITATIVELY, which is very important. Consider removing or qualifying these tables, or where possible: provide quantitative estimates of rates or volumes (as appropriate).
3-3	Table 3-1	The term solubility is inappropriate when discussing nanoparticles like MWCNT in solution. They do not dissolve in the sense of molecules. This should be changed.
3-4	Figure 3-1 and discussion	This figure omits the important phenomenon of hydrophobic organic contaminant and metal adsorption to MWCNT – this is a relevant "modification" that could affect fate/transport. It is discussed in the text but should be added to the figure.
3-9 – 3-10 (and other places)	All text	Discussion of "partitioning" of MWCNT to sediment is not thermodynamically correct. These are not molecules and so their association with particulate matter (or organic phases) is not governed by equilibrium partitioning theory (molecular-based). Instead, the association is governed by colloidal homo- and heteroaggregation theory (e.g. DLVO), such that attachment to particles may be irreversible or at least highly hysteretic. This section should be amended to reflect this critical difference between nanoparticulate contaminants such as MWCNT and molecular species such as DecaBDE.
3-16	Information Box # 8	I don't see any reason for this discussion to be "called-out" in an information box. It should be included within the main text body (this is true for many of the blue-outlined "information boxes").
4-3 and 4-10	Text box #4-1 and Information Box # 10	The information in Information Box #10 should be merged into Text Box 4-1. The discussion, information, and references are related to essentially the same general idea and topic: Analytical methods for MWCNT are immature. Within the combined text box, it should be stated EXPLICITLY that nearly all currently available methods are unsuitable for detection, characterization, and quantitation of MWCNT at ppb (or lower) concentrations in complex but important media such as soil or sediment.
4-10	Lines 10-12	The identification of CNT in the lung tissues of WTC victims was equivocal and I don't think this statement should be so strong.
5-12	DecaBDE can inform…	I'm not convinced that it is necessarily useful to draw parallels between reproductive toxic effects of DecaBDE and MWCNT, since these are going to have VERY different mechanisms.

Page	Line # or Paragraph	Comment or Question
5-22	Information box #17	This information should be included in the main text (as mentioned before for other similar boxes).
J-4 – J-12	Figures J-1, J-5, J-6	The word "degradation" is spelled incorrectly in the figures.
xxvii	Lines 19-22	These sentences are redundant (repetitive).

Review By:
Fadri Gottschalk, Ph.D.

Peer Review Comments on EPA's Draft Document
Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

Fadri Gottschalk, Ph.D.
ETSS / ETH
Zurich, Switzerland

April 2, 2013

I. GENERAL IMPRESSIONS

This document is a very thorough, well-written scientific report that reflects the extensive work done by the authors.

The report is substantial and thus requires much time reading but also to reflect on its contents. It covers—with exceptions (commented in detail below)—the relevant research, and shows that the CEA (Comprehensive Environmental Assessment) approach for analyzing the environmental implications of chemicals or engineered nanomaterial necessitates much effort on the part of the researchers; however, it may produce new evidence by combining literature knowledge with judgments of experts and other involved people.

The report, as a whole, is somewhat awkwardly organized, with many annotations and numerous text boxes, tables, and figures both in the text and appendices. I have some general points to mention—this is mostly more a wish list than a list of absolute necessities—that hopefully help the authors conduct their final edits to the report.

I. Shorten many lengthy passages distributed throughout the document, and clearly present at the beginning what work methods (embedded in CEA) contributed to this manuscript: literature review, online questioning, expert workshop, first-stage peer review, etc.

J. The reader often does not see any difference between the main text and the appendices. In both categories, the text (sometimes with similar if not the same content), tables, and even text boxes within the appendices, are dense. For me, the annexed material contains information that is important enough to be included in the body of the manuscript. Thus, I would reorganize the main copy and the appendices by keeping, for example, most of the text in the body and only tables with more or less just literature data and other documentation into the appendices. Furthermore, some text (especially some introductions to particular chapters) in the appendices seems repetitious of the corresponding introductions in the main text.

K. The manuscript may work very well in electronic form, but as a paper document only, some difficulties are present: for example, it lacks the page numbers in the table of contents (precise numbers and chapter independent page numbers).

L. I know there is a limit to how much literature research one can do and include, but I've

indicated below where there is a lack of literature (for the time period of your data search). Including it may benefit your report.

M. I found it somewhat tedious to be faced with so many intra-textual references (from back to front) to chapters that I had already read. However, these might make more sense to readers of the electronic version.

N. Research priorities were identified through the RTI workshop process and presented in a satisfactory manner in the report; however, I wonder if in this workshop quantitative parameter values were also produced that could be used directly for environmental exposure or effect assessments/modeling. Could you add a chapter, some passages, on questions such as how to organize/use expert workshops for data preparation of multimedia modeling? In addition, the reader seems to be left somewhat in the dark regarding the 13 participants in the workshop—for example, were the participants experts in all areas discussed in the workshop?

O. We know (as suggested in the first review process), that the comparison with decaBDE may either confuse or help the reader. The arguments for and against such comparison were presented in the first review. I would like to mention the "DecaBDE Can Inform MWCNT Assessment" boxes: these boxes and their idea convince me, but maybe you could be more specific when presenting the differences (and their consequences for the assessment) between these semi-volatile molecules and the carbon particles. Such clear distinction could help modelers and experimental/analytical people in using/defining the right parameters and using the right model input values.

P. I'm aware this report is not intended to serve as a basis for near-term risk decisions on the use of MWCNTs. As mentioned above, research priorities were clearly identified via this CEA. However, I wonder if from such great efforts we should not get some kind of risk results as well. The authors were very cautious and did not draw any conclusions in the context of risk estimation/evaluation. There are good reasons to be very careful, but some prudent first/rough assessments (or some references to risk results presented elsewhere) could probably be presented.

II. RESPONSE TO CHARGE QUESTIONS

Completeness and Accuracy

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

Yes, absolutely; my impression was that the authors accurately conveyed the science considered. Several spot checks on the literature I'm well familiar with did not show any inaccuracies.

I've got two critical points:

1. Completeness: I'm not saying that you have to take everything into account, but I collected the literature that I thought missing and indicated where I would place/consider such literature in the report. See below (**A**) for missing literature.

2. In the context of the comparison of MWCNT to decaBDE (i.e., justification for such a comparison), I would pay more attention to the complex issues of fate that we are faced with when assessing the environmental distribution of nanomaterials, as described several times (Christian et al. 2008; Hassellöv et al. 2008; Klaine et al. 2008; Tiede et al. 2008).

The pros and cons in comparing MWCNT to decaBDE have been comprehensively mentioned in the first review process and I do not want to repeat this; the responses/adaptations of the authors satisfy so far. However, I'm still missing a kind of introductory (immediate) explanation also from a material property perspective (well placed at the beginning, for example, in Chapter 1.1.4, Selection of DecaBDE for Comparison) as to why the comparison of MWCNT to decaBDE can be useful. It is somehow incomplete to focus on a comparison that exclusively helps identify research gaps by illustrating the manufacturing process and exposure scenarios and by understanding the process of regulating a chemical, etc.

In this context, I also wonder if the "partner chapters" G and H should be chapters of the appendices or moved to the main text. I guess you could build these two chapters in a more congruent way or rather exactly with the same structure. This would highlight similarities, differences in material properties, and data gaps. For example, in Chapter H.3.3.1, water solubility and Kow are said to be important physicochemical factors for predicting the behavior of BDE-209 in water. I agree, and of course the Kow is not applicable to non-soluble MWCNTs. Now the equivalent chapter for MWCNTs in Chapter G is not really there; however, discussion/literature on the crucial parameter "fate of carbon nanotubes" in water is not totally missing (see also literature suggestions made). Regarding Table H-3: an equivalent table—even if partially empty—for MWCNTs in Chapter G would be very interesting.

A. Literature that one should check for possible consideration (till November 2012)

A.1) Environmental fate (Chapter 1.1.4, see point 2 just mentioned above):

Hassellov, M., Readman, J.W., Ranville, J.F., Tiede, K., 2008. Nanoparticle analysis and characterization methodologies in environmental risk assessment of engineered nanoparticles. Ecotoxicology 17, 344-361.

Klaine, S.J., Alvarez, P.J.J., Batley, G.E., Fernandes, T.F., Handy, R.D., Lyon, D.Y., Mahendra, S., McLaughlin, M.J., Lead, J.R., 2008. Nanomaterials in the environment: Behavior, fate, bioavailability, and effects. Environmental Toxicology & Chemistry 27, 1825-1851.

Tiede, K., Boxall, A.B.A., Tear, S.P., Lewis, J., David, H., Hassellov, M., 2008. Detection and characterization of engineered nanoparticles in food and the environment. Food Additives and Contaminants 25, 795-821.

A.2) MWCNTs use in flame-retardant textiles (Chapters 1.3.2, 1.3.3):

Fasfous, I.I., Radwan, E.S., Dawoud, J.N., 2010. Kinetics, equilibrium and thermodynamics of the sorption of tetrabromobisphenol A on multiwalled carbon nanotubes. Applied Surface Science 256, 7246-7252.

Haiou, Y., Jie, L., Xin, W., Zhiwei, J., Yujie, W., Lu, W., Jun, Z., Shaoyun, F., Tao, T., 2011. Charing polymer wrapped carbon nanotubes for simultaneously improving the flame retardancy and mechanical properties of epoxy resin. Polymer 52, 4891-4898.

Haiou, Y., Jie, L., Zhe, W., Zhiwei, J., Tao, T., 2009. Combination of carbon nanotubes with Ni 2O 3 for simultaneously improving the flame retardancy and mechanical properties of polyethylene. Journal of Physical Chemistry C 113, 13092-13097.

Im, J.S., Bai, B.C., Bae, T.-S., In, S.J., Lee, Y.-S., 2011. Improved anti-oxidation properties of electrospun polyurethane nanofibers achieved by oxyfluorinated multi-walled carbon nanotubes and aluminum hydroxide. Materials Chemistry and Physics 126, 685-692.

Ji Sun, I., Byong Chol, B., Tae-Sung, B., Se Jin, I., Young-Seak, L., 2011. Improved anti-oxidation properties of electrospun polyurethane nanofibers achieved by oxyfluorinated multi-walled carbon nanotubes and aluminum hydroxide. Materials Chemistry and Physics 126, 685-692.

Lee, S.K., Bai, B.C., Im, J.S., In, S.J., Lee, Y.-S., 2010. Flame retardant epoxy complex produced by addition of montmorillonite and carbon nanotube. Journal of Industrial and Engineering Chemistry 16, 891-895.

Qiu, J., Zhang, S.-h., Wang, G.-j., Gong, Y.-l., 2009. Surface modification and application of multi-walled carbon nanotubes in fire-retardant coatings. New Carbon Materials 24, 344-348.

Ullah, S., Ahmad, F., 2012. Enhancing the Char Resistant of Expandable Graphite Based Intumescent Fire Retardant Coatings by using Multi-wall Carbon Nano Tubes for Structural Steel. Diffusion and Defect Data Part B (Solid State Phenomena) 185, 90-93.

Verdejo, R., Barroso-Bujans, F., Rodriguez-Perez, M.A., de Saja, J.A., Arroyo, M., Lopez-Manchado, M.A., 2008. Carbon nanotubes provide self-extinguishing grade to silicone-based foams. Journal of Materials Chemistry 18, 3933-3939.

Wang, J.-X., Jiang, D.-Q., Gu, Z.-Y., Yan, X.-P., 2006. Multiwalled carbon nanotubes coated fibers for solid-phase microextraction of polybrominated diphenyl ethers in water and milk samples before gas chromatography with electron-capture detection. Journal of Chromatography A 1137, 8-14.

Outside the review time range:

Knight, C.C., Ip, F., Zeng, C., Zhang, C., Wang, B., 2013. A highly efficient fire-retardant nanomaterial based on carbon nanotubes and magnesium hydroxide. Fire and Materials 37, 91-99.

A.3) Production volumes estimations of raw material (Chapter 2):

Piccinno F, Gottschalk F, Seeger S, Nowack B. Industrial Production Quantities and Uses of Ten Engineered Nanomaterials in Europe and the World. J Nanopart Res. 2012; 14.

Future Markets. The World Market for Carbon Nanotubes, Nanofibers, Fullerenes and POSS. Future Markets, Inc.; 2011.

A.4) Material synthesis (Chapter 2.2.2), these are all review articles:

Ying, L.S., Salleh, M.A.b.M., Yusoff, H.B.M., Rashid, S.B.A., Abd Razak, J.B., 2011. Continuous production of carbon nanotubes - A review. Journal of Industrial and Engineering Chemistry 17, 367-376.

Golnabi, H., 2012. Carbon nanotube research developments in terms of published papers and patents, synthesis and production. Scientia Iranica 19, 2012-2022.

Huang, J., Zhang, Q., Zhao, M., Wei, F., 2102. A review of the large-scale production of carbon nanotubes: The practice of nanoscale process engineering. Chinese Science Bulletin 57, 157-166.

Yanfeng, M., Bin, W., Yingpeng, W., Yi, H., Yongsheng, C., 2011. The production of horizontally aligned single-walled carbon nanotubes. Carbon 49, 4098-4110.

Kumar, M., Ando, Y., 2010. Chemical Vapor Deposition of Carbon Nanotubes: A Review on Growth Mechanism and Mass Production. Journal of Nanoscience and Nanotechnology 10, 3739-3758.

A.5) Releases during the material synthesis/handling (Chapter 2.2.2.2):

Ogura, I., Sakurai, H., Mizuno, K., Gamo, M., 2011. Release potential of single-wall carbon nanotubes produced by super-growth method during manufacturing and handling. Journal of Nanoparticle Research 13, 1265-1280.

A.6) Releases during use (Chapter 2.4.2.):

Schlagenhauf, L., Chu, B.T.T., Buha, J., Nueesch, F., Wang, J., 2012. Release of Carbon Nanotubes from an Epoxy-Based Nanocomposite during an Abrasion Process. Environmental Science & Technology 46, 7366-7372.

Liang, S., Chen, G., Peddle, J., Zhao, Y., 2012. Reversible dispersion and releasing of single-walled carbon nanotubes by a stimuli-responsive TTFV-phenylacetylene polymer. Chemical Communications 48, 3100-3102.

A.7) Waste handling, incineration (Chapter 2.5.2.):

Walser, T., Limbach, L.K., Brogioli, R., Erismann, E., Flamigni, L., Hattendorf, B., Juchli, M., Krumeich, F., Ludwig, C., Prikopsky, K., Rossier, M., Saner, D., Sigg, A., Hellweg, S., Guenther, D., Stark, W.J., 2012. Persistence of engineered nanoparticles in a municipal solid-waste incineration plant. Nature Nanotechnology 7, 520-524.

Mueller NC, Buha J, Wang J, Ulrich A, Nowack B. Modeling the flows of engineered nanomaterials during waste handling. Environmental Science: Processes & Impacts. 2013; 15(1): 251-9.

A.8) Fate in water (Chapter 3.3.):

Schwyzer I, Kaegi R, Sigg L, Smajda R, Magrez A, Nowack B. Long-term colloidal stability of 10 carbon nanotube types in the absence/presence of humic acid and calcium. Environmental Pollution.2012; 169(0): 64-73.

A.9) Ecotoxicological effects (Chapter 5.2.):

Zhu Y, Zhao Q, Li Y, Cai X, Li W. 2006. The interaction and toxicity of multi-walled carbon nanotubes with Stylonychia mytilus. J. Nanosci. Nanotechnol. 6:1357-1364.

Ghafari P, St-Denis CH, Power ME, Jin X, Tsou V, Mandal HS, Bols NC, Tang XW. 2008. Impact of carbon nanotubes on the ingestion and digestion of bacteria by ciliated protozoa. Nature Nanotechnology 3:347-351.

Schwab F, Bucheli TD, Lukhele LP, Magrez A, Nowack B, Sigg L, Knauer K. 2010. Are Carbon Nanotube Effects on Green Algae Caused by Shading and Agglomeration? Environmental Science & Technology 45:6136-6144.

Templeton RC, Ferguson PL, Washburn KM, Scrivens WA, Chandler GT. 2006. Lifecycle effects of single-walled carbon nanotubes (SWNTs) on an estuarine meiobenthic copepod. Environ. Sci. Technol. 40:7387-7393.

Roberts AP, Mount AS, Seda B, Souther J, Qiao R, Lin S, Ke PC, Rao AM, Klaine SJ. 2007. In vivo biomodification of lipid-coated carbon nanotubes by Daphnia magna. Environ. Sci. Technol. 41:3025-3029.

Cheng JP, Flahaut E, Cheng SH. 2007. Effect of carbon nanotubes on developing zebrafish (Danio rerio) embryos. Environ. Toxicol. Chem. 26:708-716.

A.10) Analytical methods for detecting, measuring, and characterizing (Appendix B):
(I know, fullerenes are not really CNT and the studies are not without controversy, but, since there's nothing else for comparison/analogies?)

Farré, M., Pèrez, S., Gajda-Schrantz, K., Osorio, V., Kantiani, L., Ginebreda, A., Barcelü, D., 2010. First determination of C60 and C70 fullerenes and N-methylfulleropyrrolidine C60 on the

suspended material of wastewater effluents by liquid chromatography hybrid quadrupole linear ion trap tandem mass spectrometry. Journal of Hydrology 383, 44-51.

Sanchis, J., Berrojalbiz, N., Caballero, G., Dachs, J., Farre, M., Barcelo, D., 2011. Occurrence of Aerosol-Bound Fullerenes in the Mediterranean Sea Atmosphere. Environmental Science & Technology 46, 1335-1343.

Clarity and Use of Priority Areas to Support Research Planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

Yes. Basically, priority research areas are highlighted very well in the report. The text boxes throughout are well organized and color-coded: red refers to the so-called priority areas for research, grey to unprioritized areas, and green boxes are used for the decaBDE–MWCNT comparison. However, numbering and indexing for those boxes is missing, making it difficult to read the report as a hard copy.

The Importance/Confidence Matrices are clear and easy to understand. But I wonder if a more detailed textual analysis of these matrices' based output would provide the basis for a research paper to be extracted from this report. Unfortunately, having only 13 participants is not enough for statistical evaluation, and the competences of the participants are not really discussed. Furthermore, I'm not sure whether it makes sense that the authors only present in Chapter 6—Chapter 6.3, with the participants' rationale for designating the areas, shows the outcomes of the prioritization process in more detail—the identification of these priority areas by expert stakeholders that in the end represents the crucial part for connecting risk research, assessment, and management. Since these outcomes have been used to focus the information in the whole case study, should this information not be included as a key part of the report already at the beginning?

Another point is that even if the additional information highlight boxes (with scientific concepts related to the priority areas), as well as the other figures and tables, refer to priority research areas (Boxes 6 and 7 refer, for example, explicitly to issues covering such areas), the organizational relationship between the different boxes (figures and tables) seems to me not too apparent in the report. A table description with reference to the areas, for example, for Table 6-3, and directly appended to the table (and not only in the main text body), would help. The same kind of intra-textual references/indications on the interconnections are also needed for the green boxes, since these boxes reveal how data on decaBDE should be used for MWCNT research planning that is focused on these priority areas.

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

Please see the literature suggestions made above under Question 1 that have been grouped by the different research areas.

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

Yes, this goal is achieved. However, it will be important to evaluate the missing literature (please see the comments above, Charge Question 1) to exclude that, until now, not considered (possibly conflicting) results would inform research planning differently. Second, at the end of the green boxes, concrete research questions are listed in each case to inform MWCNT research planning in the identified priority areas. I'm wondering if it would make sense to collect and prioritize all these concrete questions/instructions for researchers in a summary or conclusion table, box, or figure. The same question arises for all conclusions made on research planning outside of the comparison of decaBDE to MWCNT.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

As partially mentioned in my introductory comments, I would suggest the authors look at:

- numbering and indexing all chapters, boxes, tables, and figures
- creating more transparent and consistent organization regarding the alternating between decaBDE and MWCNT in the text and document structure, which at present seems discordant
- numbering and indexing all pages in the hard copy
- declaring explicitly and at the beginning of this manuscript how the authors distinguish between content for Appendices E and F and Chapter 3; Appendix F and Chapters 4 and 5; Appendices G, H, and Chapter 6; and Appendix G and Chapters 2–5
- explicitly declaring at the beginning of the manuscript the use and purpose of the different kinds of boxes
- condensing the annotations and possibly moving relevant annotated text (as proposed above) into the main document
- condensing lengthy passages
- removing any extraneous cross-references in the text between the chapters, especially when later chapters refer back to earlier ones

Responses to Public and Peer Comments on the MWCNT Case Study ERD

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

Yes.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

Yes, my impression is that the authors took the comments seriously and did a very good job revising the manuscript and responding to the suggestions/comments.

Some remaining suggestions:

Missing current literature: There are still some additional studies on MWCNTs that possibly should be included (please see above comments).

Critique on the comparison with decaBDE: As mentioned above, this comparison needs some additional legitimation, and an introductory explanation from a material property perspective, as to why the comparison of MWCNT to decaBDE is meaningful.

Missing gray literature: I know the report cannot fully present an exhaustive review of all the literature. However, I would tell the reader in more detail how peer review, non-peer review, and gray literature, etc., were treated.

As suggested once, I also think that the authors could possibly add a final concluding chapter or remarks by giving some prudent statements on risk assessment that go beyond the modest purpose of identifying and prioritizing research gaps.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

Please see comments on Questions 6 and 7.

Potential Utility of Knowledge Maps

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of

a pilot project to visually convey information in presented in CEA case study documents more concisely.

Yes, absolutely. However, at the end of the appendix, I'd like to see some discussion or conclusion concerning the objective of this subproject that was to develop methods (for visually and concisely presenting information) in CEA.

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

Yes, if the model input data classification (known, not available, and similar descriptions) is used for all maps and if this classification reflects the newest evidence available. If not, this leads to misleading conclusions and non-legitimate decisions in this context.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

Basically, yes. These maps are based on Table 3-1 and Table H-3 and transform information in tabular form into figures, like flow charts. Figure J-2 reflects Table H-3; however, this table is based on old and more non-quantitative data for MWCNTs—there is newer (partially contradicting) evidence available, as listed above. I would adapt this figure by considering these data or at least, for example, the modeling studies on MWCNT and environment that the authors referred to in Table 3-2. The same applies to Map J-4.

Terrestrial box: Is a distinction of natural, agricultural, and urban soils meaningful/feasible?

I know the figures already contain a legend; however, I think that a clear map description directly appended to the table would facilitate analysis and understanding.

III. SPECIFIC OBSERVATIONS

Page	Line # or Paragraph	Comment or Question
22	4	Possibly also consider the European definition* of nanomaterials based on their primary particle size. *EU. Commission Recommendation of 18 October 2011 on the definition of nanomaterials. Official Journal of the European Union; 2011. p. 38-40.
22 and 34		P. 22 *"Although no national or international consensus definition for nanomaterials exists, a current working definition is a material having at least one dimension on the order of 1 to 100 nm (NSTC, 2011)."*

Page	Line # or Paragraph	Comment or Question
		P. 34 *"Nanoscale materials (nanomaterials) have been described as having at least one dimension 1 approximately 1–100 nm (NSTC, 2011)."* I had several times—when reading through the whole document— the impression of having already read; this is only the first of such passages. I have not inventoried them. Please see also next comment and the generic remark above on lengthy.
34	9-23	This passage (or identical content) is—as an example—given at least three times throughout the document. Please see p. 34, p. 22, p. 25, p. 40, p. 484
36		The CEA framework and process (principal elements) are explained too intensively (and mostly from a general perspective) throughout the manuscript; this wearies the reader.
37	Figure 1-1	The groundwater compartment is missing. I would not be too secure about the harmlessness of engineered nanomaterial in groundwater. Based on the judgment of experts and the fact that there are hardly any data on that compartment, I would discuss this problem. See e.g.: Colvin, V.L., 2003. The potential environmental impact of engineered nanomaterials. Nature Biotechnology 21, 1166-1170. U.S. House Committee on Science. Hearing on Societal Implications of Nanotechnology, April, 2003. 108th Congress (House Committee on Science, Washington, DC, 2003.
40	12	Why such a source (Boner, 2011) on drug-delivery systems in this context? The other source is more realistic, however, about partnering with universities as a choice for nanotechnology start-up firms (Wang and Shapira, 2012).
43	22	Boxes outlined in red and gray are not numbered and not listed in any directory?
45	1	Why are these kind of chapters not numbered in the manuscript? ***How the Case Study Was Revised to Respond to Public and Peer Comments***
45	Figure 1.3	Upper left part of the figure is not clear and unreadable.
46	Title	*1.1.4. Selection of DecaBDE for Comparison* Title and text do not correlate, the text is something else. It is more on impacts of decaBDE on ecological and human health.
47	16	Missing source after *"Although commercial MWCNT flame-retardant*

Page	Line # or Paragraph	Comment or Question
51	Additional Information Highlight Box 1	*products are available, their presence is 16 relatively new, and they are by no means abundant on the market."* and in Highlight Box 1.
59	1	*"…physicochemical properties might drive these differences and to what degree ~~are not fully understood~~. …degree needs to be investigated"*
59	Text Box 1-1	Is Johnston et al.(2010) the only source for this whole box on physicochemical properties and fate? Possibly consider: Aschberger, K., Johnston, H.J., Stone, V., Aitken, R.J., Hankin, S.M., Peters, S.A.K., Tran, C.L., Christensen, F.M., 2010. Review of carbon nanotubes toxicity and exposure-Appraisal of human health risk assessment based on open literature. Critical Reviews in Toxicology 40, 759-790.
61	Additional Information Highlight Box 2	Köhler et al. (2008) do not really treat flame-retardant textiles. I would not refer to this study in this box. However, Schubauer-Berigan et al. (2011), Nicolas Messin (Nanocyl) (2012) seem up to date,. Can you extract more from them? I wonder if the authors could provide in the main text some concrete values on the MWCNT use/production amounts for the U.S.?
70	Figure 2-1	1. Should the authors also consider textile manufacturing that is not restricted only to the incorporation of the flame retardant substances into the textiles? 2. End of Life: Reuse of products containing decaBDE and MWCNTs is clear for me. But, I can hardly imagine reuse, recycling and disposal of decaBDE and MWCNTs?
73	First Box	Numbering and indexing for Prioritized and Unprioritized Research Area Boxes are missing.
82	5-6	*"The release of other substances used during purification is also possible."* This sentence is isolated and alone. Are there sources or/and other examples of such substances that may be released?
90	1-3	*"Environmental releases are expected from upholstery textiles coated with flame retardants due to 1 (1) the potential use scenarios for the upholstery textiles and (2) the physicochemical properties of MWCNTs."* Is this a meaningful sentence? Or should it be *Environmental release is influenced by…*
90	24	I do not know of any studies on MWCNT for such release, but I'm

Page	Line # or Paragraph	Comment or Question
		asking if you should mention here available experimental/analytical release studies performed for other engineered nanomaterials? Benn, T.M., Westerhoff, P., 2008. Nanoparticle Silver Released into Water from Commercially Available Sock Fabrics. Environmental Science & Technology 42, 4133-4139. Geranio, L., Heuberger, M., Nowack, B., 2009. The Behavior of Silver Nanotextiles during Washing. Environmental Science & Technology 43, 8113-8118. Windler, L., Lorenz, C., von Goetz, N., Hungerbuehler, K., Amberg, M., Heuberger, M.P., Nowack, B., 2012. Release of titanium dioxide from textiles during washing. Environmental Science & Technology 46, 8181-8188.
101	6-7	*"In general, information on environmental concentrations of MWCNTs was not found."* This contradicts, for example, what is presented in Table 3-2.
102	Box	*"What concentrations..."* Should you refer to Table 3-2?
127	Chapter 4.1.2.2.	Perhaps you can also extract some values from: Koelmans, A.A., Nowack, B., Wiesner, M.R., 2009. Comparison of manufactured and black carbon nanoparticle concentrations in aquatic sediments. Environmental Pollution 157, 1110-1116.
140	Box	*"…likely would be released from upholstery textiles in the particulate phase, in a manner similar to BDE-209 (Nowack et al., 2012)"* Is Nowack et al. 2012 the right source here?
150	Title	4.3. Ecological Exposure… *Ecological* seems in the whole manuscript to be used as a synonym for *environmental*, however, environment is used as well. Is such use consistent?
175	2-3	*"For aquatic ecosystems, little information was identified for MWCNTs; conversely, much information was identified on the potential effects of MWCNTs in terrestrial ecosystems."* Is it not just the other way around? This seems wrong to me, I added above several ecotoxicological literature on aquatic systems (see please comments above). Please find here a few terrestrial studies: Scott-Fordsmand JJ, Krogh PH, Schaefer M, Johansen A. 2008. The

Page	Line # or Paragraph	Comment or Question
		toxicity testing of double-walled nanotubes-contaminated food to Eisenia veneta earthworms. Ecotoxicology and Environmental Safety 71:616-619.63. Atieh MA, Fakhru'l-Razi A, Girun N, Chuah TG, El-Sadig M, Biak DRA. 2006. Effect of multi-wall carbon nanotubes on the mechanical properties of natural rubber. Composite Structures 75.
187	6-23	5.3.3. Climate Change Is this chapter really necessary? I would not refer to climate dynamics. This link is—as the authors said—totally unclear (unnecessary?) from a scientific perspective.
189	11-16	Why not add also some recommendations regarding making industrial nanomaterial production and application volumes transparent?
206	Table 6-7	Could the authors give an insight into the estimation procedure/method of finances and time frame?
383 384	12, 23 7	*"No data are available on MWCNT concentrations in..."* These statements contradict what is presented in Chapter 3.5, e.g. Table 3-2.
386 and 387		No numbering and indexing for titles: *Toxicokinetics and Body Burden in Aquatic Systems* *Toxicokinetics and Body Burden in Terrestrial Systems*

Review By:
Stig I. Olsen, Ph.D.

Peer Review Comments on EPA's Draft Document
Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

Stig I. Olsen, Ph.D.
Toxicon v/Stig Olsen
DK-2880 Bagsvaerd
Denmark

April 5, 2013

I. GENERAL IMPRESSIONS

The document is well structured and cross-referencing links within the document are a highly appreciated feature. Overall, the accuracy is good (to my knowledge). Clarity of presentation sometimes suffers due to the length of the text; however, often the information is also presented in an overview in tables which is very good. But it would also be good to summarize after each chapter.

The whole process of the CEA is thoroughly described and provides a very good introduction to the remainder of the document, as well as to the terminology used. Also, the previous steps of the current document are adequately described and give the reader a good understanding of why the document is built as it is. However, a good understanding of the framework, as such, was for me better achieved after reading Chapters 6.1 and 6.2.

Figure 1-3 provides a very good overview of the results of the collective judgment prioritization process.

The relatively long introduction and explanation of flame retardancy is not at all times very relevant to CEA—I would reduce it to a few pages explaining the principles of MWCNT for flame retardancy and providing the perspectives of potential volumes and thus releases—and put the remainder in an appendix.

Additional highlight boxes work well in conveying the additional information and are in most instances relevant.

It is a bit confusing that LCA is mixed up a bit with risk assessment—it is clear that e.g. the feedstock may not be of importance for risk assessment of MWCNT, but in an LCA it can be of importance due to other types of emissions, resource usage, etc. Likewise in the manufacturing, there will be extensive use of solvents to refine the MWCNT or reagents for functionalization—which are not taken into account in the CEA (except to a minor extent in Chapter 4.5 "cumulative exposures") but would be in an LCA (as well as the waste material/by-products from the refining). It is stressed several times, e.g. on page 5.1 lines 3-7, that the CEA framework includes other impacts than toxicological—however, this is not at all well communicated in the document as a whole. The whole Chapter 2 on the product life cycle could

have put a lot more weight on these issues rather than just being briefly mentioned in Chapter 5.3.
Areas in which there is no information are often not mentioned, i.e. it should be clearly stated that in order to actually do an assessment we would need this information. An example is Chapter 3.3 where nothing is mentioned about stability and transformation in water and sediment.

The conclusions are generally sound.

II. RESPONSE TO CHARGE QUESTIONS

Completeness and Accuracy

1. Is the science accurately conveyed throughout the document? If not, (1) please list any areas that need improvement and (2) provide specific comments/revisions that will more accurately convey the science.

Generally, I find that the science is accurately conveyed. A few comments to Chapter 5 are:

Page 5-29 - the review of Eckelman et al. (2012) lacks the essential information that, when applying the USEtox framework, the authors make adaptations in order to handle the CNTs. USEtox is developed for organic chemicals and will probably not be suitable for CNTs. This could be a factor to consider in their results.

In Chapter 5.3.3, I don't necessarily think there is an unclear relationship between climate change and production of MWCNT. The high CO2 in Khanna et al. is due to the energy consumption and, considering the high energy consumption listed earlier, there will be huge climate change impacts related to all production pathways.

Chapter 6.3.4.4 lacks reflections on the gaps in knowledge regarding broad environmental considerations (life cycle assessments).

Clarity and Use of Priority Areas to Support Research Planning

2. Are the priority areas identified by previous experts that reviewed the MWNCT Case Study ERD and participated in the workshop process clearly highlighted throughout the document? Throughout the document, areas of the CEA framework are highlighted if they were identified as priority areas (i.e., areas important to consider in future risk assessments of MWCNTs but generally lacking confidence in the current state of the science to support risk management decisions) by previous experts that reviewed the MWNCT Case Study ERD and participated in a workshop process, "Nanomaterial Case Studies Workshop Process: Identifying and Prioritizing Research for Multiwalled Carbon Nanotubes."

I find that the boxes presenting "prioritized" or "unprioritized" research areas are very illustrative and very clearly highlight the opinions of previous experts.

3. For the priority areas that have been highlighted, do you know of any additional existing studies specific to MWCNTs that should be included in the case study to help develop research plans that subsequently support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

I think that the incineration part (Chapter 2.5.2.2) is relying too much on anticipation that MWCNT will be oxidized in incineration. A few papers I have (included at the bottom of this review) do not clearly indicate that this is so. And even controlled incineration has clumps of waste that are not fully incinerated or where the temperature does not reach maximum.

4. Does the content of the document support research planning to inform future assessment and risk management efforts for MWCNTs? If not, please provide specific revisions that would improve the utility of the document for research planning to support future assessment and risk management efforts of MWCNTs.

I find that the document is very supportive in future research planning. Chapter 6 makes a good conclusion on the process.

In Chapter 5 it would be very helpful to have a table that better summarizes the studies mentioned in the text. Table 5-1 is not very helpful (it almost says there are no data on anything) since there are useful results from a range of studies. Tables 5-2 and 5-3 convey much more useful information.

5. Is the organization of the document logical, and does it facilitate comprehension and understanding? If not, please provide specific organizational revisions that would improve the comprehension and understanding.

The overall structure is logical. However, as previously mentioned, I find that the information in Chapters 6.1 and 6.2 would be better placed in Chapter 1 to give a better understanding of the purpose of the document.

Responses to Public and Peer Comments on the MWCNT Case Study ERD

6. Are comments from peer and public stakeholders who reviewed the MWNCT Case Study ERD transparently conveyed and clearly summarized (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey comments.

They are comprehensively and transparently conveyed.

7. Are EPA responses to comments transparently and clearly conveyed (i.e., original comments making up comment themes can be easily identified, comment themes are readily identifiable and understandable) in Appendix I? If not, please provide specific revisions to more transparently and clearly convey EPA responses.

I find that the comments and responses have been thoroughly described in Appendix I. I particularly like that the comments and responses have been grouped and thus provide a better overview of how the EPA has responded to the comment. This makes it more transparent and clear.

8. In revising the case study document, is it evident that EPA was responsive to input from stakeholders and made appropriate changes to the document? If not, please state any specific instance(s) in which EPA did not respond appropriately and how the response could be revised to respond appropriately.

It is evident that EPA has been responsive to the comments.

Potential Utility of Knowledge Maps

9. Is the rationale and selected approach for the pilot project described in Appendix J clear? If not, please indicate specific points that could be clarified. Appendix J presents the results of a pilot project to visually convey information in presented in CEA case study documents more concisely.

The rationale is OK as described. I find that the knowledge maps provide very good visual information. I must admit that the text in itself didn't provide a good understanding of the structures of the figures with nodes and edges until I saw the figures (but maybe that's my English that does not suffice). Furthermore, the text (and maybe the figures as well?) lacks good explanation of what is the "weight of evidence" for the information conveyed regarding the l Physicochemical Properties Map (PPM). There is a mix-up between 'varying parameters' and 'unknowns' in my understanding. And the purple "potential," does that represent lack of evidence or what? How is it represented that there is no knowledge?

10. As a whole, do the Transport, Transformation and Fate Knowledge Maps presented in Appendix J facilitate the identification of knowledge gaps for MWCNTs? If not, please provide specific revisions to the approach that could improve the identification of knowledge gaps for MWCNTs.

I think that the TfM and TpM clearly illustrate the limited knowledge on MWCNT environmental fate. The same clarity is missing in the PPM. I don't have good ideas for how to improve this.

11. Do each of the maps (i.e., Physicochemical Properties, Transport, and Transformation Maps for decaBDE and MWCNT) in Appendix J accurately and clearly present information conveyed in Chapter 3 and related appendices on Transport, Transformation, and Fate? If not, please list specific revisions to improve the accuracy or clarity of the maps.

Figure J-2 seems to lack potential coating/functionalization and the consequences of this. But apart from this, I believe they do summarize the information given in other parts of the document.

III. SPECIFIC OBSERVATIONS

Page	Line # or Paragraph	Comment or Question
J-2	18	It refers to Table 3-2 that has the environmental concentrations, whereas it should refer to Table 3-1.
J-4	Figure J-1	Confusing that lipophilicity and Kow are separated— just use one of them.
J-12	Figure J-6	An explanation for MWCNT is missing.
xxvii	19-22	Repetition of sentence.
1-11	15-17	The reader is left curious about which "three instances" there was disagreement between stakeholders—either refer to another place in the document where this is explained or place a footnote explaining this.
1-22	Table 1-5	The table should also indicate where MWCNT are placed—with application methods and mechanisms.
2-4	Figure 2-2	The figure is a bit misleading since releases to the environment may also occur from the material processing and product manufacturing. Would be better to have the "environment" to the right and the application running through all life cycle stages.
5-6	Table 5-1	You should double check that the crosses are still in the right place, e.g. it is strange that the cross for reproductive/developmental is under no data when there are some studies??

References

Additional references on thermal stability:

Sui, YC et al. (2001). Structure, thermal stability, and deformation of multibranched carbon nanotubes synthesized by CVD in the AAO template. J Phys Chem B 105(8): 1523-1527.

Cataldo, F.(2002). A study on the thermal stability to 1000°C of various carbon allotropes and carbonaceous matter both under nitrogen and in air. Fullerenes, Nanotubes and Carbon Nanostructures . 10(4): 293-311.