SUPPLEMENTAL MATERIAL

for "**Evaluating the Mechanistic Evidence and Key Data Gaps in Assessing the Potential Carcinogenicity of Carbon Nanotubes and Nanofibers in Humans**,"

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Supplement Contents

Table S-1. DNA damage in tissues of animals after exposure to carbon nanotubes (*in vivo* studies)

Material[a]	Exposure	Effect	Reference
MWCNT (NM400: Nanocyl, D: 5-35 nm, L: 0.7-3.0 µm, SSA: 298 m^2/g; NM402: Akema, Graphistrangth C100, D: 6-20 nm, L: 0.7-4.0 µm, SSA: 225 m^2/g)	25.6 µg/week for 5 weeks in *ApoE* knockout mice. Total dose = 128 µg/mouse	Increased levels of SB and unaltered FPG-sensitive sites in lungs (comet assay). Increased expression levels of *Ogg1* in lung tissue	Cao et al. (2014)
MWCNT (D: 44 nm, L: 2.7 µm, SAA: 69 m^2/g, 5.3% Fe) from Nikkiso Co. Ltd (Tokyo, Japan)	0.2 or 1 mg/kg (aqueous solution with 1% Tween 80), or 0.04 or 0.2 mg/kg once a week for 5 weeks by i.t. instillation in rats and sacrifice at 3 or 24 h after the last exposure	Unaltered levels of SB in lungs (comet assay). Increased level of SB following exposure to positive control (ethyl methane sulfonate)	Ema et al. (2013b)
SWCNT (D: 0.9-1.7 nm, L: less than 1 µm, SSA: 731 m^2/g, 2% Fe) from Thomas Swan and Co Ltd (Consett, UK)	0.064 or 0.64 mg/kg by oral gavage in rats and sacrifice at 24 h after the administration	Increased levels of 8-oxodG (HPLC-ECD) in lung and liver; unaltered levels in colon mucosa cells. Unaltered expression level of *Ogg1* in lung and liver. Unaltered OGG1 activity in liver tissue	Folkmann et al. (2009)
MWCNT (D: 7-15 nm, L: 0.5-200 µm) from Sigma-Aldrich	2, 5 or 10 mg/kg by intraperitoneal injection in Swiss albino mice and sacrifice at 3 h after the exposure	Increased levels of SB in bone marrow cells after the exposure to low doses (2 and 5 mg/kg, comet assay). Excluded from the study because genotoxicity has been measured in a non-target tissue	Ghosh et al. (2011)
SWCNT (D: 0.8-1.2 nm, L: 0.1-1 µm, less than 23% Fe, from CNI, Houston, TX, USA; D: 1.2-2 nm, L. 1-15 µm, 0.05% Fe, from SES Research, Houston, TX, USA)	50 µg/week for 6 weeks by i.t. instillation (PBS with 0.05% Tween 80) in mice with allergic pulmonary inflammation (ovalbumin sensitized) or normal counterparts	Increased levels of 8-oxodG in lung tissue (assessed by immunohistochemistry). The study has been excluded from the review because the measurement of genotoxicity is based on an unspecific assay	Inoue et al. (2010)
SWCNTs (D: less than 1 µm, L: 0.9-1.7 nm, SSA: 731 m^2/g) from Thomas Swan and Co. Ltd. (Consett, UK)	54 µg/mouse (saline with 10% BALF) by i.t. instillation and sacrifice at 3 or 24 h after the exposure	Increased levels of SB in BALF at 3 h (comet assay)	Jacobsen et al. (2009)
MWCNT (D: 90 nm, L: 2 µm) from Mitsui & Co., Ltd	50 or 200 µg/mouse by i.t. instillation and	Increased levels of SB (comet assay) and lipid peroxidation product-derived DNA adducts in	Kato et al. (2013)

Table S-1. DNA damage in tissues of animals after exposure to carbon nanotubes (*in vivo* studies)

Material[a]	Exposure	Effect	Reference
(Ibaraki, Japan). Designated MWCNT-7	sacrifice at 3 h (comet assay) or 3, 24, 72 or 168 h (8-oxodG) after exposure	lungs. Levels of 8-oxodG was reported to be increased, but the baseline levels of DNA lesions was rather high (approximately 4.8 lesions/10^6 nucleotides, corresponding to 22 lesions/10^6 dG)	
MWCNT (D: 10-15 nm, L: 20 µm, SSA: 225 m^2/g, 2% Fe) from Hanwha Nanotech. Inc (Icheon, Korea)	0.16, 0.34 or 0.94 mg/m^3 (6 h/day) for 5 days in rats and sacrifice immediately or 1 month days after the last exposure	Increased levels of SB in lungs (comet assay) immediately (1.5-fold) and 1 month (1.3-fold) after the last exposure.	Kim et al. (2012)
MWCNT (D: 10-15 nm, L: 330 nm, SSA: 225 m^2/g, 2% Fe) from Hanwha Nanotech. Inc (Icheon, Korea)	0.17, 0.49 or 0.96 mg/m^3 (6 h/day and 5 days/week) by nose-only inhalation for 28 days F344 in rats and sacrifice immediately or 90 days after the last exposure	Dose-dependent increased level of SB in lungs (comet assay) immediately (lowest dose) and day 90 (middle and high dose) after the last exposure. Larger effect on SB levels was observed immediately after the exposure (2.4-fold) as compared to the later time point (1.4-fold)	Kim et al. (2014)
SWCNT (D: 1.8 nm, L: 4.4 µm, SSA: 878 m^2/g, 4.4% Fe) from Nikkiso Co. Ltd (Tokyo, Japan)	0.2 or 1 mg/kg (aqueous solution with 1% Tween 80), or 0.04 or 0.2 mg/kg once a week for 5 weeks by i.t. instillation in rats and sacrifice at 3 or 24 h after the last exposure	Unaltered levels of SB in lungs (comet assay). Increased levels of SB in lung tissue after exposure to positive control (ethyl methanesulfonate)	Naya et al. (2012)
MWCNT (D: 12 nm, L: up to 12 µm, SSA: 41-42 m^2/g) from NanoLab (Newton, MA, USA) as either non-functionalized or functionalized (acid treated) materials	0.25-0.75 mg/kg (saline with 1% Tween 80) once a day for five days by intraperitoneal injection in mice and sacrifice at 24 after the last exposure	Dose-dependent increase in SB levels in peripheral blood leukocytes (comet assay). Excluded from the study because genotoxicity has been measured in a non-target tissue	Patlolla et al. (2010)

Table S-1. DNA damage in tissues of animals after exposure to carbon nanotubes (*in vivo* studies)

Material[a]	Exposure	Effect	Reference
MWCNT (L: 1.1 µm, D: 12 nm, SSA: 226 m^2/g, 3% Al, 2.7% Fe) from Arkema, Colombes, France (Graphistrength C100)	0.05, 0.25 or 0.5 mg/m3 (6 h/day, 5 days/week) for 90 days in Wistar rats. Sacrificed 24 h after the last exposure	Unaltered levels of SB (comet assay) in lungs, kidney and liver. Addition of hOGG1 indicated no additional oxidized sites in exposed rats. There is concern about the reliability of this measurement of hOGG1-sites because the positive control for DNA strand breaks (MMS) also showed increased levels of hOGG1-sites, but MMS does not directly generate lesions that are recognized by hOGG1	Pothmann et al. (2015)
MWCNT NRCWE-026 (Nanocyl NC7000) "CNTSmall". 14.9% Al_2O_3, 0.29% Fe_2O_3, 0.11% CoO; L: 0.85 ± 0.457 µm; D: 11 ± 4.5 nm. SSA: 245.8 m^2/g MWCNT NM-401 (IO-LE-TECNanomaterials) "CNTLarge". 0.14% P_2O_5, 0.05% Fe_2O_3, 0.08% CO_3. L: 4.05 ± 2.40 µm; D: 67 ± 26.2 nm. SSA: 14.6 m^2/g	0, 18, 54, 162 µg/mouse by intratracheal instillation. Lungs collected 24 h, 3 and 28 days post-exposure	SB (comet assay). CNTSmall enhanced the level of DNA strand breaks at the middle and high dose on post-exposure day 3. CNTLarge enhanced at all doses at post-exposure day 1 only	Poulsen et al. (2015)
SWCNT (D: 0.9-1.7 nm, L: less than 1 µm, SSA: 731 m^2/g, 2% Fe) from Thomas Swan and Co. Ltd (Consett, UK)	0.5 mg/kg administered at 26 and 2 h before sacrifice (in saline with 10% BALF, total dose = 1 mg/kg) in *ApoE* knockout mice	Unaltered levels of SB and FPG-sensitive sites (comet assay) in lungs. Unaltered expression of *Ogg1* in lung tissue	Vesterdal et al. (2014b)
MWCNT described as "short" (D: 15 nm, L: 3 µm) or "long" (D: 150 nm, L: 8 µm)	0.125 mg/rat once every other week for 24 weeks (total dose = 1.6 mg/kg) and sacrifice at 24 h after the last exposure	Increased levels of 8-oxodG in lung tissue [the detection method was not described and the basal levels of 8-oxodG (1.3 ng/mg DNA) corresponds to 7600 lesions/10^6 dG, assuming the molecular weight of 8-oxodG is 283 g/mol and 1 fmol/µg DNA is equal to 1.64 lesions/10^6 dG).Excluded from the review because it has a high background level of 8-oxodG, suggesting a flawed	Xu et al. (2014)

Table S-1. DNA damage in tissues of animals after exposure to carbon nanotubes (*in vivo* studies)

Material[a]	Exposure	Effect	Reference
		methodology	

[a] Nanomaterial characteristics include tube diameter (D), length (L), specific surface area (SSA) and content of transition metals.

Source: Adapted from Table 1 in Section 4.3 of IARC monograph 111 (IARC, in press), which was originally developed by authors on this paper. Table S-1 has been restructured, and two new studies have been added: Pothmann et al., 2015; Poulsen et al., 2015 and Vesterdal et al., 2014b.

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
SWCNT (D: 1.2-1.7 nm, L: 0.3-0.5 µm) (characteristics have been obtained from the Sigma catalogue)	5-20 µg/ml for 24-48 h in HepG2 cells	Concentration-dependent increase in the levels of SB at both exposure times (comet assay)	Alarifi et al. (2014)
MWCNT as pristine ((D: 67 nm, L: 1.1 µm, SSA: 60 m^2/g, (0.5% Fe) from Mitsui Chemicals (Kawasaki-Shi, Japan) or purified form with low Fe content (D: 70 nm, L: 1.2 µm, SSA: 52 m^2/g, 0.03% Fe).	50 µg/cm^2 for 24 h in murine alveolar macrophages (MH-S cells)	Increased levels of SB after exposure to pristine MWCNTs and unaltered levels in cells after exposure to MWCNT with low Fe content (comet assay)	Aldieri et al. (2013)
MWCNT defined as "short"(D: 7-180 nm, L: 1-5 µm) and "long" (D: 8-177 nm, L: 0.1-20 µm), synthetized for the study	20-200 µg/ml for 24 h in rat kidney epithelial (NRK-52E) cells	Increased levels of SB (comet assay) after exposure to "long" tubes (levels of SB in unexposed cells have not been reported). DNA damage by exposure "short" tubes was reported to be non-significant (data not shown). No effect on generation of DSB (γH2AX by immunostaining)	Barillet et al. (2010)
SWCNT (L: 5 µm, 50-70% pure) from Sigma Aldrich	10 µg/ml for 24 h in microvascular endothelial cells	Unaltered levels of SB (comet assay). The study lacks a true positive control for the comet assay, although the authors show that exposure to nanosized TiO_2 was associated with increased levels of SB	Bayat et al. (2015)
MWCNT (D: 20-40 nm, L: 0.5-200 µm, 0.55% Fe) from Heji Inc. (Hong Kong, China)	5-100 µg/ml for 2-24 h in A549 cells	Increased levels of SB (comet assay). Unaltered levels of FPG-sensitive sites [uncertainty about the result because of lack of positive control]	Cavallo et al. (2012)
MWCNT (D: 13-18 nm, L: 1-5 µm, 99% pure) from Cheap Tubes Inc (Battleboro, VT) as pristine form or functionalized as hydroxylated-oxygenation, carboxylated or amidated	20 mg/ml for 24 h in BEAS-2B cells	Functionalized forms increased the level of SB, whereas the pristine form did not (comet assay). The study is excluded from the review because of uncertainty about the number of independent replicates in the experiment	Chatterjee et al (2014)
SWCNT (D: 0.8-12 nm, L: several microns, 0.62% Fe) from Sigma	50-200 µg/ml for 96 h in rat aortic endothelial cells	Concentration-dependent increase levels of SB (comet assay). The study has been excluded from the review because of	Cheng et al. (2012)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
		uncertainty about replicates being independent experiments	
SWCNT (D:1.6 nm, L: 0.8 µm, SSA: 407 m^2/g, 10% impurities) from Cheaptubes (USA)	50-150 µg/ml for 24 h in human gingival fibroblasts	Increase levels of SB (comet assay)	Cicchetti et al. (2011)
MWCNT (D: 20-40 nm, L: 1-5 µm, 1% impurities) and SWCNT (30% impurities) as either pristine or amide-functionalized samples	25 µg/ml for 44 h in human lymphocytes	Increased level of DSB (γH2AX immunostaining)	Cveticanin et al. (2010)
SWCNT 1100 purified, Nanocyl (D :1.5-4 nm ; L : >1 µm), 3.15% Si; 1.44%Co; 0.14%Mg, SSA : 1128 m^2/g	0.23-3.75 µg/cm^2 for 24 h in SHE cells and V79 fibroblasts	Unaltered levels of SB (comet assay)	Darne et al. (2014)
MWCNT 3100 purified, Nanocyl (D: 11-12 nm; L: 1.5 µm), 0.22% Fe; 0.1% Co, SSA : 333 m^2/g	0.23-3.75 µg/cm^2 for 24 h in SHE cells and V79 fibroblasts	Unaltered levels of SB (comet assay)	Darne et al. (2014)
MWCNT 3150 purified, Nanocyl (D: 15-19 nm; L: <1 µm). 0.21% Fe, SSA : 308 m^2/g	0.23-3.75 µg/cm^2 for 24 h in SHE cells and V79 fibroblasts	Unaltered levels of SB (comet assay)	Darne et al. (2014)
MWCNT SBb raw, LMSPC UMR 7515 (D: 15-68 nm; L: >0.8 µm), 7.22% Al; 4.15% Fe, SSA : 151 m^2/g	0.23-3.75 µg/cm^2 for 24 h in SHE cells and V79 fibroblasts	In SHE cells: Increased levels of SB (comet assay) concentration-dependent; significant at 1.87, 3.75 µg/cm^2. Increased levels of Fpg-sensitive sites In V79 fibroblasts: Unaltered levels of SB	Darne et al. (2014)
MWCNT SBp purified, LMSPC UMR 7515 (D: 9-77; L: > 0.8 µm). 0.86% Fe, SSA : 168 m^2/g	0.23-3.75 µg/cm^2 for 24 h in SHE cells and V79 fibroblasts	In SHE cells: Increased levels of SB (comet assay) concentration-dependent; significant at 1.87, 3.75 µg/cm^2. Increased levels of Fpg-sensitive sites at 3.75µg/cm^2 In V79 fibroblasts: Unaltered levels of SB	Darne et al. (2014)
MWCNT (D: 10-25 nm, L: 0.5-50 µm, SSA: 400 m^2/g, 1.5% Ni) and SWCNT (D: 1.2-1.5 nm, L: 2-5 µm, SSA:	3-50 µg/ml for 24 h in RAW 264.7 cells	Bell-shaped concentration-response relationship for induction of SB after exposure to MWCNT (peak at 3 µg/ml) and SWCNT (peak at 10 µg/ml) (comet assay)	Di Giorgio et al. (2011)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
400 m^2/g, 1.5% Ni) from Sigma			
MWCNT (D: 7-15 nm, L: 0.5-200 µm) from Sigma-Aldrich	2-10 µg/ml for 3 h in human lymphocytes	Increased levels of SB at 2 µg/ml, but not 1, 5 and 10 µg/ml (comet assay)	Ghosh et al. (2011)
MWCNT (D; 30 nm, L: less than 1 µm, 3.4% Ni, 0.13% Fe) from Lawrence Berkeley National Laboratories (Berkeley, CA)	0.5-20 µg/ml for 6, 12 or 24 h in human umbilical vein endothelial c 8vells (UVECs)	Increased level of DSB (γH2AX immunostaining)	Guo et al. (2011)
MWCNTs, including MWCNT-7 (D: 74 nm, L: 5.7 µm, SSA: 24-28 m^2/g, 99% pure, Mitsui or Hodogaya) and various OECD materials (NM400, NM401, NM402 and NM403)	12.5-200 µg/ml for 24 h in MML FE1-MutaTMmouse lung epithelial cells	Only increased levels of SB after one type of MWCNT out 15 materials (COOH-functionalized material from Cheaptubes with a diameter of 8-15 nm, length of 10-50 µm and SSA of 233 m^2/g)	Jackson et al., (2015)
SWCNT (D: 0.9-1.7 nm, L: less than 1 µm, SSA: 731 m^2/g, 2% Fe) from Thomas Swan (Consett, UK)	100 µg/ml for 3 h in murine FE1-MML lung epithelial cells	Unaltered levels of SB and increased levels of FPG-sensitive sites (comet assay)	Jacobsen et al. (2008)
MWCNT (D: 30 nm, L: less than 1 µm, 3.4% Ni, 0.13% Fe) from Lawrence Berkeley National Laboratories (Berkeley, CA, USA)	0.3-30 µg/ml for 2-24 h in A549 cells	Unaltered levels of DNA damage (neutral comet assay)	Ju et al. (2014)
MWCNT (D: 100-200 nm, L: 3-7 µm) from Sigma	20-40 µg/cm^2 for 4 h in A549 cells	Increased levels of SB and unaltered levels of FPG-sensitive sites (comet assay). Other particle types (e.g. ZnO and CuO) increased levels of FPG-sensitive sites, indicating reliable methodology	Karlsson et al. (2008)
MWCNT (NM400: Nanocyl, D: 5-35 nm, L: 0.7-3.0 µm, SSA: 298 m^2/g; NM402: Akema, Graphistrangth C100, D: 6-20 nm, L: 0.7-4.0 µm, SSA: 225 m^2/g)	5-20 µg/cm^2, for 4 h in human hepatoblastoma (C3A) cells	Increased levels of SB (comet assay). FPG-modified assay showed increased the levels of DNA lesions. Subtraction of SB levels from the total sites after FPG treatment indicates positive values of FPG-sensitive sites (regarded as a positive genotoxic effect	Kermanizadeh et al. (2012)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
		in this review)	
MWCNT (NM400: Nanocyl, D: 5-35 nm, L: 0.7-3.0 µm, SSA: 298 m^2/g; NM402: Akema, Graphistrangth C100, D: 6-20 nm, L: 0.7-4.0 µm, SSA: 225 m^2/g)	1.25-5 µg/cm^2 for 4 h in human renal proximal tubule epithelial (HK-2) cells	Increased levels of SB (comet assay). FPG-modified assay showed increased the levels of DNA lesions. Subtraction of SB levels from the total sites after FPG treatment indicates negative values of FPG-sensitive sites (regarded as a null effect finding in this review)	Kermanizadeh et al. (2013)
SWCNT (D: 1-1.2 nm, L: 20 µm) from Hanwha Nanotech (Incheon, Korea)	25-100 µg/ml for 24-48 h in phytohemagglutinin-stimulated human lymphocytes	Increased levels of SB, which was blunted by treatment with N-acetylcysteine (comet assay)	Kim & Yu (2014)
MWCNT (D: 10-15 nm, L: 0.2 µm, <2% Fe, <2% Co, <4% Al_2O_3, SSA: 225 m^2/g) from Hanwha Nanotec Inc., Incheon, Korea	12.5-50 µg/ml for 24-48 hy in human lymphocytes	Increased levels of SB (comet assay) after 24 h (12.5-50 µg/ml) and 48 h (25 and 50 µg/ml)	Kim et al., (2016)
SWCNT (D: 0.4-1.2 nm, L: 1-3 µm, SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc. (Houston, TX, USA)	24-96 µg/cm^2 for 3-24 h in lung fibroblasts (V79)	Increased levels of SB (comet assay). Decreased viability at the same concentrations as elevated DNA damage	Kisin et al. (2007)
SWCNT (D: 0.4-1.2 nm, L: 1-3 µm, SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc. (Houston, TX, USA)	24 or 48 µg/cm^2 for 3-24 h in lung fibroblasts (V79)	Increased levels of SB (comet assay)	Kisin et al. (2011)
Mixed CNT (50% SWCNT and 40% other nanotubes, D: 1.1 nm, L: 0.5-100 µm) from Sigma	1-100 µg/cm^2 for 24-72 h in human BEAS-2B cells	Increased levels of SB (comet assay)	Lindberg et al. (2009)
MWCNT (D: 10-30 nm, L: 1-2 µm) and SWCNT (D: less than 2 nm, L: 1-5 µm) from SES Research (Houston, TX, USA)	5-200 µg/cm^2 for 24-72 h in BEAS-2B or human mesothelial (MeT-5A) cells	Increased levels of SB (comet assay) at 24 h (BEAS-2B and Met-5A, 5-200 µg/cm^2) by exposure to SWCNT. Increased levels of SB by exposure to MWCNT in MeT-5A cells (comet, 48 h). SWCNT increased the levels of M1dG (immune-slot blot) in BEAS-2B and Met-5A cells after 48 h exposure, whereas there were decreased levels after 72	Lindberg et al. (2013)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
		h exposure (MeT-5A). MWCNT exposure decreased the levels of M1dG in MeT-5A cells (72 h)	
MWCNT (characteristics not reported) from New Jersey Institute of Technology (NJ, USA). The MWCNTs were used as pristine, purified and COOH-functionalised samples	20 µg/ml for 4-24 h in human keratinocytes (HaCaT)	Unaltered levels of SB and increased levels of FPG total sites (comet assay). Subtraction of SB levels from the total sites after FPG treatment indicates positive values of FPG-sensitive sites (regarded as a positive genotoxic response in this review). Excluded from the review because of insufficient information about fiber characteristics	McShan & Yu (2012)
MWCNT (D: 110-170 nm, L: 5-9 µm, SSA: 22 m^2/g, less than 0.1% Fe) and SWCNT (D: 0.7-1.2 nm, L: 0.5-100 µm, SSA: 400 m^2/g) from Sigma	1-100 µg/ml for 24 h in RAW 264.7 cells	Increased levels of SB, ENDOIII- and FPG-sensitive sites for both SWCNT and MWCNT. Similar induction of DNA damage by both types of CNTs (comet assay)	Migliore et al. (2010)
MWCNT from Bussan Nanotech Research, Ibaraki, Japan. Fiber characteristics have not been reported, except from a statement that the average size was 7.4 µm	5 µg/ml for 12 h in chicken DT40 lymphoid cells	Increased number of 8-oxodG and γH2AX positive cells (immunostaining). Excluded from the review because of insufficient characterization of fibers	Mohiuddin et al. (2014)
MWCNT (L: 0.5-2 µm, more than 95% purity) from Cheap Tubes Inc (Battleboro, VT) as pristine material or COOH-functionalized	50-200 µg/ml for 24 h in A549 cells	Unaltered γH2AX response (immunostaining)	Mrakovcic et al. (2015)
SWCNT (L: 0.5-2 µm, more than 90% purity) from Cheap Tubes Inc (Battleboro, VT) as pristine material or COOH-functionalized	50-200 µg/ml for 24 h in A549 cells	Unaltered γH2AX response (immunostaining) in cells exposed to the pristine material, whereas carboxylated SWCNTs showed positive response at the highest concentration (250 µg/ml)	Mrakovcic et al. (2015)
SDS-solubilized SWCNTs (fibre characteristics not reported) prepared by own	8 µg/ml for 24 h in rat kidney tubular (NRK 52E) cells	Increased levels of SB (comet assay, measured as tail moment). Image documentation indicates a very high level of	Nam et al. (2011)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
procedure		DNA damage with virtually all DNA in the tail, which seems unrealistic. The study has been excluded due to incomplete fibre characterization	
SWCNT (D: 10-30 nm) from a local source	3 h exposure in human embryonic cells (concentration is not reported)	Increased level of SB (comet assay). Excluded from the review because individual comets have been regarded as independent experiments	Nikitina et al. (2015)
SWCNT (D: less than 2 nm, L: 5-15 µm) and MWCNT (D: 10-30 nm, L: 5-15 µm) from SES Research	20 µg/ml for 8 or 24 h in human Met-5A cells	Increased levels of SB (comet assay) and unaltered levels of 8-oxodG (HPLC-ECD). Excluded from the review because the statistical analysis has been based on the total number of comets and high basal level of 8-oxodG in controls (8 lesions/10^6 dG)	Ogasawara et al. (2012)
SWCNT (D: 1.4 nm, L: 2-5 µm, SSA: 293 m^2/g, 0.07% Fe) from National Institute of Standards and Technology (Gaithersburg, MD, USA)	25-50 mg/cm^2 for 24 h in human mesothelial cells	Increased levels of SB (comet assay). Immunostaining for γH2AX was reported to be "nominal increased" (approximately 1.2-fold compared to controls). This result has been regarded as a null effect finding on generation of DSB	Pacurari et al. (2008)
SWCNT (D: 1.8 nm, L: 0.5 µm) synthetized by own procedure	10 pg/ml – 0.2 µg/ml for 3-24 h in human colon carcinoma (HT29) cells	Increased levels of SB. Incubation with FPG did not increase the levels above that of SB (comet assay)	Pelka et al. (2013)
MWCNT (D: 6-24 nm, L: 2-5 µm, impurities: less than 0.4%) from Bayer Technologies Service	7.5-30 µg/ml for 24 or 72 h in human lung A549 cells	Unaltered levels of SB (comet assay)	Thurnherr et al. (2011)
MWCNT (D: 32 nm, L: 0.07-7.8 µm, SSA: 107 m^2/g, 0.55% Fe, 1.86% Ni) or COOH-functionalized form (D: 25 nm, L: 0.03-1.56 µm, SSA: 139 m^2/g, 1.09% Co) from Heji (China)	1-40 µg/ml for 24 h in A549 or BEAS-2b cells	Increased level of SB (40 µg/ml) in A549 cells to both types of MWCNTs. Increased level of SB in BEAS-2B cells after exposure to pristine (10 and 40 µg/ml) and COOH-functionalized form (40 µg/ml). No effect on FPG-sensitive sites (hydrogen peroxide as positive control)	Ursini et al. (2014)
SWCNT (D: 0.9-1.7 nm, L: less than 1 µm, SSA: 731	25 µg/ml for 3 h in HepG2 cells	Increased levels of SB and FPG-sensitive sites (comet assay)	Vesterdal et al. (2014a)

Table S-2. DNA damage in cell cultures after exposure to carbon nanotubes (*in vitro* studies)

Material[a]	Dose and Cells	Effect	Reference
m^2/g, 2% Fe) from Thomas Swan (Consett, UK)			
MWCNT (D: 15-30 nm, L: 10-20 µm) from own production as pristine or COOH-functionalized material	12.5 µm/ml for 1 h in A549 cells	Increased level of SB and FPG-sensitive sites (comet assay)	Visalli et al. (2015)
MWCNTs (D: 20-60 nm, 5-15 µm, Meijo Nano Carbon Co. Ltd, Aichi, Japan; D. 60-100 nm, D: 1-2 µm, SES Research, Houston, TX, USA; D: less than 10 nm, L: 12 µm, SES Research) and SWCNT (D: less than 2 nm, L: 5-15 mm)	50 µg/ml for 3 h in human A549 cells	Increased levels of SB by two different MWCNTs, whereas one type of MWCNT and SWCNT did not increase the levels of SB (comet assay, data reported as tail length and tail moment). The study has been excluded from the review because individual comets have been regarded as independent experiments	Yamashita et al. (2010)
SWCNT (D: 12 nm, L: less than 5 µm, less than 1% impurities)	5 µg/ml for 24 h in primary embryo mouse fibroblasts	Increased levels of SB (comet assay)	Yang et al. (2009)
SWCNT (D: 1.1 nm, L: 50 µm, 3.7% impurities) from Heji Inc. (Hong Kong, China)	1-10 µg/ml for 6 h in human leukocytes	Unaltered levels of SB (comet assay). The study has been excluded from the review because the statistical analysis has been based on the total number of comets	Zeni et al. (2008)
MWCNT from Tsinghua and Nanfeng Chemical Group Cooperation, China (TEM pictures displayed individual tubes, although with possibility to estimate the length)	24 h exposure in mouse embryonic stem cells (concentration not specified)	Increased immunostaining for γH2AX. Excluded from the review because of insufficient information about fiber characteristics	Zhu et al. (2007)

[a]Nanomaterial characteristics include tube diameter (D), length (L), specific surface area (SSA) and content of transition metals.

Note: DNA damage (comet assay) induced by three samples of DWCNT was investigated in SHE cells and V79 fibroblasts exposed to 5 concentrations (0.23-3.75 µg/cm^2 for 24h (Darne et al 2014). Two samples (DWCNT 2100 purified, Nanocyl: D: 3-7 nm; L: 1-10 µm, 2.69% Mo; 1.79% Fe; 0.16% Si; 0.11%Ca. SSA : 626 m^2/g, and DWCNT/DWEF purified: 80% DW, 15% SW; 5%TW), CNRS 5085, D: 1.6-3.4 nm; L: 1-20 µm. 9.5% Co. SSA : 985 m^2/g) did not altered the levels of SB in both cell types. Another sample : DWCNT 2150 purified, Nanocyl, D: 3-7 nm; L: >1 µm, 2.48% Mo; 1.40% Fe; 0.10% Si; 0.12% Ca. SSA : 611 m^2/g enhanced the levels of SB at 1.87, 3.75µg/cm^2, with unaltered levels of Fpg-sensitive sites, in SHE cells, but had no effect in V79 fibroblasts.

Source: Adapted from Table 3 in Section 4.3 of IARC monograph 111 (IARC, in press), which was originally developed by authors on this paper. Table S-2 is limited to studies from human and rodent cells; it has been restructured; some of the study

entries have been revised; and several new studies have been added: Bayat et al., 2015; Chatterjee et al., 2014; Cveticanin et al., 2010; Darne et al., 2014; Guo et al., 2011; Jackson et al., 2015; Kim et al., 2016; Mrakovcic et al., 2015; Nam et al., 2011; Ursini et al., 2014; Visalli et al., 2015; Zhu et al., 2007. Certain studies have been updated with information on DNA double strand breaks (γH2AX assay), which was not thoroughly covered in the IARC monograph (Barillet et al., 2010; Mohiuddin et al., 2014; Pacuari et al., 2008).

Table S-3. Micronucleus frequency, chromosomal aberrations and mutations in tissues from animals after exposure to carbon nanotubes (*in vivo* studies)

Material[a]	Exposure	Effect	Reference
SWCNT (D: 1.8 nm, SSA: 878 m^2/g, 4.4% Fe) from Nikkiso Co. Ltd (Tokyo, Japan)	5-20 mg/kg (PBS with 1% Tween 80) by oral gavage once a day for 2 days in ICR mice, and sacrificed at 24 h after the last administration	Unaltered frequency of micronucleated immature erythrocytes in bone marrow cells. Excluded because the effect has been measured in non-target tissue	Ema et al. (2013a)
MWCNT (D: 7-15 nm, L: 0.5-200 µm) from Sigma-Aldrich	2, 5 or 10 mg/kg by intraperitoneal injection in Swiss albino mice and sacrifice at 3 h after the exposure	Increased MN frequency in bone marrow cells and unaltered percentage of polychromatic erythrocytes. Excluded because the effect has been measured in non-target tissue	Ghosh et al. (2011)
MWCNT (D: 90 nm, L: 1-4 µm, peak at 2 µm) from Mitsui & Co (Ibaraki, Japan). Designated MWCNT-7	0.2 mg/mouse as a single i.t. instillation, two instillations with 2 weeks apart, or 4 instillation (once/week for 4 weeks) and sacrifice 8-12 weeks after the last instillation in *gpt* delta mice	Increased mutation frequency in the *gpt* locus in lung tissue after 4 i.t. instillations. The predominant mutagenic event was G:C to C:G transversions. No mutagenic effect after 1 or 2 instillations	Kato et al. (2013)
MWCNTs with "short" (D: 10-15 nm, L: 150 nm, SSA: 195 m^2/g, 99% pure) or "long" (D: 10-15 nm, L: 10 µm, SSA: 178 m^2/g, 95% pure) fiber length from Hanwha Nanotech (Incheon, Korea)	12.5-50 mg/kg (PBS with 1,2-dipalmitoyl-sn-glycero-3-phosphocholine) by intraperitoneal injection in ICR mice and sacrifice at 24 h	Unaltered frequency of polychromatic erythrocytes in bone marrow cells. Excluded because the effect has been measured in non-target tissue	Kim et al. (2011)
MWCNT (D: 1.0-1.2 nm, L: 20 µm, 3% Co, 3% Ni, 1.5% Fe)	25-100 mg/kg (PBS with 1,2-dipalmitoyl-sn-glycero-3-phosphocholine) by intraperitoneal injection in ICR mice and sacrifice at 24 h	Unaltered frequency of polychromatic erythrocytes in bone marrow cells. Excluded because the effect has been measured in non-target tissue	Kim et al. (2015)
SWCNT (D: 3 nm, L: 1.2 µm, SSA: 1064 m^2/g) from National Institute of Advanced Industrial Science and Technology (Japan)	60 or 200 mg/kg (PBS with 1% Tween 80) by oral gavage once a day for 2 days in CD-1 mice, and sacrificed at 24 h after the last administration	Unaltered frequency of micronucleated polychromatic erythrocytes in bone marrow cells. Excluded because the effect has been measured in non-target tissue	Naya et al. (2011)
MWCNT (D: 11 nm, L: 0.7 µm, 2% impurities) from	0.5 and 2 mg/rat (saline with 1% Tween 80) and sacrifice at	Increased MN frequency in type II pneumocytes, occurring concurrently with	Muller et al. (2008a)

Nuclear Magnetic Resonance at the Facultés universitaires Notre-Dame de la Paix (Namur, Belgium)	day 3 after administration	pulmonary inflammation (assessed as increased number of macrophages and neutrophils in bronchoalveolar lavage fluid)	
MWCNT (D: 12 nm, L: up to 12 µm, SSA: 41-42 m^2/g) from NanoLab (Newton, MA, USA) as either non-functionalized or functionalized (acid treated) materials	0.25-0.75 mg/kg (saline with 1% Tween 80) once a day for five days by intraperitoneal injection in mice and sacrifice at 24 h after the last exposure in mice	Dose-dependent increase in structural CA (chromatid and isochromatid types of gaps, breaks, fragments, centric fusions and dicentric chromosomes) in peripheral blood lymphocytes. Dose-dependent increase in MN frequency femoral bone marrow cells. Excluded because the effect has been measured in non-target tissue	Patlolla et al. (2010)
MWCNT (L: 1.1 µm, D: 12 nm, SSA: 226 m^2/g, 3% Al, 2.7% Fe) from Arkema, Colombes, France (Graphistrength C100)	0.05, 0.25 or 0.5 mg/m^3 (6 h/day, 5 days/week) for 90 days in Wistar rats. Sacrificed 24 h after the last exposure	Unaltered micronuclei frequency (micronucleated polychromatic erythrocytes). Excluded because the effect has been measured in non-target tissue	Pothmann et al. (2015)
SWCNT (D: 0.8-1.2 nm, L: 0.1.1 µm, SSA: 508 m^2/g, 17.7% Fe, 0.16% Cu, 0.05% Cr, 0.05% Ni) from Carbon Nanotechnology (CNI, Houston, TX)	Inhalation (5 mg/m^3, 5 h/day for 4 days) or pharngyal aspiration (5-20 µg/mouse) in C57BL/6 mice at day 1, 7 or 28 after the last exposure	Enhanced pulmonary mutation frequency in the K-*ras* locus in mice after inhalation of SWCNTs (post-exposure days 7 and 28). Pharynheal aspiration did not alter the mutation frequency	Shvedova et al. (2008)
SWCNT (D: 65 nm, L: 1-3 µm, SSA: 1040 m^2/g, 0.23% Fe) from Unidym (Sunnyvale, CA)	5 mg/m^3 (5 h/day for 4 day, total dose = 5 µg/mouse) or pharyngeal aspiration (40 µg/mouse) in C57BL/6 mice. Sacrifice 1year after the last exposure	Inhalation of SWCNTs was associated with increased level of MN in lung tissue. The exposure increased mutation frequency in lung tissue (K-ras mutations in codon 8 and 12)	Shvedova et al. (2014)

[a]Nanomaterial characteristics include tube diameter (D), length (L), specific surface area (SSA) and content of transition metals.

CA, chromosome aberrations; MN, micronucleus

Source: Adapted from Table 2 in Section 4.3 of IARC monograph 111 (IARC, in press), which was originally developed by authors on this paper. Table S-3 includes similar content but has been restructured, and several new studies have been added: Kato et al., 2012; Kim et al., 2015; Pothmann et al., 2015; Shvedova et al., 2008; Shvedova et al., 2014.

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
MWCNT (D: 88 nm, L: 5 µm) from Mitsui & Co Ltd. (Tokyo, Japan). Designated MWCNT-7	0.02-5 µg/ml for 24 h in Chinese hamster lung cells	Concentration-dependent increase in the number of MN (Cochran-Amitage trend test), especially related to bi- and multinucleated cells. Slightly reduced growth index (63% at highest concentration). Polyploid chromosome number. No structural chromosomal changes. Unaltered levels of mutations in the *hgprt* locus	Asakura et al. (2010)
Gd-SWCNT (no information about fibre characteristics)	50 µg/ml for 48 h in mouse embryonic fibroblasts (NIH/3T3)	Unaltered MN frequency (CBPI not reported). The study has been excluded due to incomplete fibre characterization	Avti et al. (2013)
SWCNT (D: 2 nm, L: 1-5 µm, SSA: 436 m^2/g) and MWCNT (D: 10-30 nm, L: 1-2 µm, SSA: 60 m^2/g) from SES Research, Houston, TX, USA	6.25-300 µg/ml in human lymphocytes for 24, 48 or 72 h and harvested 24 h after the exposure	Increased chromatid-type (48 h) and chromosome-type (48 and 72 h) breakage following exposure to SWCNT (300 µg/ml). Chromatid-type (24 h) and chromosome-type (48 h) breakage following exposure to MWCNT (50 µg/ml)	Catalan et al. (2012)
SWCNT (D:1.6 nm, L: 760 nm, SSA: 407 m^2/g, 10% impurities) from Cheaptubes (USA)	50-150 µg/ml for 24 h in human gingival fibroblasts	Bell-shaped concentration response curve (CBMN, maximal MN frequency at100 µg/ml). Decreased CBPI at high concentrations	Cicchetti et al. (2011)
MWCNT (D: 20-40 nm, L: 1-5 µm, 1% impurities) and SWCNT (30% impurities) as either pristine or amide-functionalized samples	25-150 µg/ml for 44 h in human lymphocytes	Increased MN frequency (CBMN) by MWCNT and SWCNTs (both pristine and functionalized form). Decreased CBPI at high concentrations	Cveticanin et al. (2010)
SWCNT 1100 purified, Nanocyl, (D :1.5-4 nm ; L : >1 µm), 3.15% Si; 1.44%Co; 0.14%Mg. SSA : 1128 m^2/g	5 concentrations: 0.23-3.75 $\mu g/cm^2$ for 24h in SHE cells (PDT: 14-18h) and fibroblasts V79 (PDT: 18-20h)	In SHE cells: Unaltered MN frequency. Unaltered mitotic index In V79 fibroblasts: Increased MN frequency at 2 concentrations (0.94; 1.87 $\mu g/cm^2$). Unaltered mitotic index	Darne et al. (2014)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
MWCNT 3100 purified, Nanocyl (D: 11-12 nm; L: 1.5 µm), 0.22% Fe; 0.1% Co. SSA : 333 m^2/g	5 concentrations: 0.23-3.75 µg/cm^2 for 24h in SHE cells (PDT: 14-18h) and fibroblasts V79 (PDT: 18-20h)	In SHE cells: Increased MN frequency at 0.47µg/cm^2. Unaltered mitotic index In V79 fibroblasts: Increased MN frequency at the 3 concentrations (0.23; 0.94; 1.87 µg/cm^2). Decreased mitotic index	Darne et al. (2014)
MWCNT 3150 purified, Nanocyl (D: 15-19 nm; L: <1 µm). 0.21% Fe. SSA : 308 m^2/g	5 concentrations: 0.23-3.75 µg/cm^2 for 24h in SHE cells (PDT: 14-18h) and fibroblasts V79 (PDT: 18-20h)	In SHE cells: Increased MN frequency at 3 concentrations (0.23; 0.94; 1.87 µg/cm^2). Unaltered mitotic index In V79 fibroblasts: Increased MN frequency at the 4 concentrations (0.23; 0.94; 1.87; 3.75 µg/cm^2). Decreased mitotic index	Darne et al. (2014)
MWCNT SBb raw, LMSPC UMR 7515 (D: 15-68 nm; L: > 0.8 µm), 7.22% Al; 4.15% Fe. SA : 151 m^2/g	5 concentrations: 0.23-3.75 µg/cm^2 for 24h in SHE cells (PDT: 14-18h) and fibroblasts V79 (PDT: 18-20h)	In SHE cells: Increased MN frequency at 4 concentrations (no increase at the highest concentration). Decreased mitotic index In V79 fibroblasts: Increased MN frequency dose-response. Decreased mitotic index	Darne et al. (2014)
MWCNT SBp purified, LMSPC UMR 7515 (D: 9-77; L: > 0.8 µm). 0.86% Fe. SSA : 151 m^2/g	0.23-3.75 µg/cm^2 for 24h SHE (PDT: 14-18h)	In SHE cells: Increased MN frequency at 3 lowest concentrations (0.23; 0.47; 0.94 µg/cm^2). Decreased mitotic index In V79 fibroblasts: Increased MN frequency dose-response. Decreased mitotic index	Darne et al. (2014)
MWCNT (D: 10-25 nm, L: 0.5-50 µm, SSA: 400 m^2/g, 1.5% Ni) and SWCNT (D: 1.2-1.5 nm, D: 2-5 µm, 1.5% Ni) from Sigma	1-10 µg/ml for 24-72 h in rat RAW 264.7	Concentration-dependent increase in micronuclei (CBMN) formation after 48 h incubation (same effect of SWCNT and MWCNT). Increased percentage of cells with chromosome damage including, acentric fragments, centrometric	Di Giorgio et al. (2011)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
		fusion, breaks, loss of protein, chromatid separation and polyploidy	
MWCNT (D: 110-170 nm, L: 5-7 µm, SSA: 130 m^2/g, less than 0.1% Fe)	*Salmonella typhimurium* TA 98 and TA 100 strains, and *Escherichia coli* WP2uvrA strains	Absence mutagenic effect at any concentration in absence or presence of S9 mix	Di Sotto et al. (2009)
SWCNT (D: 1.8 nm, SSA: 878 m^2/g, 4.4% Fe) from Nikkiso Co. Ltd (Tokyo, Japan)	6.25-100 µg/ml for 6 or 24 h in Chinese hamster lung fibroblast cells (CHL/IU) *Salmonella typhimurium* TA97, TA98, TA100 and TA1535 strains, and *Escherichia coli* WP2uvrA/pKM101 strains	Unaltered response in terms of chromosomal gaps and polyploidy Unaltered mutation frequency in bacteria absence or presence of S9 mix	Ema et al. (2013a)
SWCNT (D: 0.9-1.7 nm, L: less than 1 µm, SSA: 731 m^2/g, 2% Fe) from Thomas Swan (Consett, UK)	100 µg/ml for 576 h in murine FE1-MML lung epithelial cells	Unaltered levels of mutagenicity in the *cII* locus	Jacobsen et al. (2008)
MWCNT (D: 90 nm, L: 1-4 µm with a peak at 2 µm) from Mitsui & Co., Ltd (Ibaraki, Japan). Designated MWCNT-7	20 µg/ml for 6 h in A549 (micronucleus assay) or for 1 h in CHO AA8 cells (SCE assay)	Increased MN frequency (A549 cells). Growth index = 70% Increased levels of SCE (CHO AA8 cells)	Kato et al. (2013)
MWCNT (D: 10-15 nm, L: 0.15 or 10 µm, SSA: 178 or 195 m^2/g, 1% or 5% iron) from Hanwha Nanotech (Incheon, Korea)	1.6-12.5 µg/ml in Chinese hamster ovary (CHO-k1) cells for 24 h *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 strains, and *Escherichia coli* WP2uvrA strains	Unaltered response in terms of chromatid-type breakage or exchange, and chromosome-type breakage of exchange Unaltered mutation frequency in bacteria in absence or presence of S9 mix	Kim et al. (2011)
SWCNT (D: 1-1.2 nm, L: 20 µm, 3% Co, 3% Ni, 1.5% Fe) from Hanwha Nanotech (Incheon, Korea)	12.5-50 µg/ml for 24 h in Chinese hamster ovary (CHO-k1) cells *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 strains, and *Escherichia coli* WP2uvrA	Unaltered response in terms of chromatid-type breakage or exchange, and chromosome-type breakage of exchange Unaltered mutation frequency in bacteria in absence or presence of S9 mix	Kim et al. (2015)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
	strains		
MWCNT (D: 10-15 nm, L: 0.2 µm, <2% Fe, <2% Co, <4% Al_2O_3, SSA: 225 m^2/g) from Hanwha Nanotec Inc., Incheon, Korea	12.5-50 µg/ml for 28 h in human lymphocytes (24 h incubation with cytochalasin B)	Concentration-dependent increase MN frequency (CBMN, unaltered CBPI)	Kim et al. (2016)
SWCNT (D: 1-1.2 nm, L: 20 µm) from Hanwha Nanotech (Incheon, Korea)	25-100 µg/ml for 20 min in phytohemagglutinin-stimulated human lymphocytes	Increased MN frequency (CBMN, unaltered CBPI)	Kim & Yu (2014)
SWCNT (D: 0.4-1.2 nm, L: 1-3 µm, SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc. (Houston, TX, USA)	12-96 µg/cm^2 for 24 h in hamster lung fibroblasts (V79) cells *Salmonella typhimurium* YG1029 and YG1024	Limited (not statistically significant) increase in MN formation (maximal 70% cytotoxicity) Unaltered mutation frequency in bacteria in absence or presence of S9 mix	Kisin et al. (2007)
SWCNT (D: 0.4-1.2 nm, L: 1-3 µm, SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc. (Houston, TX, USA)	12-48 µg/cm^2 for 24 h in hamster lung fibroblasts (V79)	Increased number of MN (24 h, 12-24 µg/cm^2, cell medium)	Kisin et al. (2011)
Mixed CNTs (more than 50% SWCNTs and 40% other nanotubes, D: 1.1 nm, L: 0.5-100 µm) from Sigma	1-100 µg/ml (or 3.6-360 µg/cm^2) for 24, 48 or 72 h in human BEAS-2B	Unaltered MN frequency (CBMN, unaltered CBPI)	Lindberg et al. (2009)
SWCNT (D: less than 2 nm, L: 1-5 µm) and MWCNT (D: 10-30 nm, L: 1-2 µm) from SES Research (Houston, TX, USA)	80-200 µg/cm^2 in human BEAS-2B cells for 48 or 72 h	Unaltered MN frequency (CBMN, decreased CBPI at high concentrations)	Lindberg et al. (2013)
SWCNTs with short (D: 1-2 nm, L: 0.4-0.8 µm, SSA: 585 m^2/g), medium (D: 1-2 nm, L: 1-3 µm, SSA: 337 m^2/g) or long (D: 1-2 nm, L: 5-30 µm, SSA: 310 m^2/g) fibers with little content of impurities	1-100 µg/ml for 24-48 h in BEAS-2B or for 24 h in MCL-5 cells	Increased MN frequency (CBMN) in both BEAS-2B and MCL-5 lymphoblastoid cells (unaltered CBPI) Increased level of mutations in the *hprt* locus after exposure to medium-length SWCNTs in MCL-5 cells (other samples did not increase the mutation frequency)	Manshian et al. (2013)
SWCNT (D: 0.7-1.2 nm, L: 0.5-100 µm, SSA: 400 m^2/g) and MWCNT (D:	0.01-100 µg/ml for 44 h in murine macrophages	Concentration-dependent increased MN frequency (CBMN) with	Migliore et al. (2010)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
110-170 nm, L: 5-9 µm, SSA: 22 m^2/g, less than 0.1% Fe) from Sigma	(RAW 264.7)	unaltered CBPI. MWCNTs had effect at lower concentration than SWCNTs (0.1 versus 1 µg/ml), whereas MWCNTs seemed to generate stronger effect than SWCNTs (2.5-fold versus 2.0-fold)	
MWCNT from Bussan Nanotech Research, Ibaraki, Japan. Fiber characteristics have not been reported, except from a statement that the average size was 7.4 µm	5 µg/ml for 12 h in chicken DT40 lymphoid cells	Increased number of chromatid and isochromatid damage. Excluded from the review because of insufficient characterization of fibers	Mohiuddin et al. (2014)
MWCNT (L: 0.5-2 µm, more than 95% purity) from Cheap Tubes Inc (Battleboro, VT) as pristine material or COOH-functionalized	50-200 µg/ml for 24 h in V79 cells	Unaltered *hgprt* mutation frequency (increased mutation frequency in positive control, ENU). Unaltered MN frequency in V79 (CBMN) and A549 cells (only tested in the absence of cytochalasin B (increased response in positive control, mitomycin C).	Mrakovcic et al. (2015)
SWCNT (L: 0.5-2 µm, more than 90% purity) from Cheap Tubes Inc (Battleboro, VT) as pristine material or COOH-functionalized	50-200 µg/ml for 24 h in V79 cells	Concentration-dependent increased level of *hgprt* mutation frequency for SWCNT (200 µg/ml) and COOH-SWCNT (50-200 µg/ml). Unaltered MN frequency in V79 (CBMN) and A549 cells (only tested in the absence of cytochalasin B (increased response in positive control, mitomycin C.	Mrakovcic et al. (2015)
MWCNT (D: 11 nm, L: 0.7 µm, 2% impurities) from Nuclear Magnetic Resonance at the Facultés universitaires Notre-Dame de la Paix (Namur, Belgium)	10-50 µg/ml in human epithelial (MCF-7) cells for 24 h or in rat lung epithelial (RLE) cells for 48 h	Concentration-dependent increase MCF-7 cells (MN assay with *in situ* hybridization using a pancentrometric probe), with no clear concentration-dependent effect on CBPI. Concentration dependent increase in RLE cells (MN assay)	Muller et al. (2008a)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
MWCNT (D: 20-50 nm, L: 0.7 µm, 0.48% Fe, 0.49% Co) that were ground to produce structural defects and/or heating (2400°C) to eliminate metals	10-50 µg/ml in rat lung epithelial (RLE) cells for 48 h	Ground MWCNTs increased MN frequency, whereas a ground and heating sample did not increase MN frequency. MWCNTs that were heated and subsequently ground increased the MN frequency (CBMN, unaltered CBPI)	Muller et al. (2008b)
SWCNT (D: 3 nm, L: 1.2 µm, SSA: 1064 m^2/g) from National Institute of Advanced Industrial Science and Technology (Japan)	300-1000 µg/ml for 24 h in Chinese hamster lung fibroblast cells (CHL/IU) *Salmonella typhimurium* TA97, TA98, TA100, TA1535 and *Escherichia coli* WpvurA/pKM101	Unaltered response in terms of chromosomal gaps and polyploidy Unaltered mutation frequency in bacteria	Naya et al. (2011)
SWCNT (D: 10-30 nm) from a local source	24-48 h exposure in human embryonic cells (concentration is not reported)	Unaltered levels of cells with aberrant metaphases, micronuclei and aneuploidy (chromosome 1, 6, 8, 11, X, Y). Excluded from the review because of untertainty about independent replication on different days	Nikitina et al. 2015
SWCNT (D: 1.8 nm, L: 0.5 µm) synthetized by own procedure	10 pg/ml – 0.2 µg/ml for 24 h in hamster lung fibroblast (V79) cells	Unaltered MN frequency, assessed by similar number of kinetochore-negative cells in SWCNT and control groups	Pelka et al. (2013)
MWCNT (D: 9.5 nm, L: 1.5 µm, 90% pure) as pristine material or COOH-, NH_2-, or OH-functionalized products from Nanocyl S.A. (Belgium)	1-100 µg/ml for 24 h in mouse fibroblasts (Balb/3T3) cells	Unaltered MN frequency (CBMN). No cytotoxicity	Ponti et al. (2013)
SWCNT (D: 1.0 nm, L: 1.0 µm) SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc. (Houston, TX, USA)	24-96 $\mu g/cm^2$ for 24 h in primary human respiratory epithelial cells (SAEC) or BEAS-2B	A significant dose response of aneuploidy, and multipolar mitotic spindles.	Sargent et al. (2009)
SWCNT (D: 1.0 nm, L: 1.0 µm) SSA: 1040 m^2/g, 0.23% Fe) from CNI, Inc.	0.024-24 $\mu g/cm^2$ for 24 h in primary human	A significant concentration response of aneuploidy which included an	Sargent et al. (2012)

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
(Houston, TX, USA)	respiratory epithelial cells (SAEC) or BEAS-2B	equal number of chromosome losses and gains of chromosomes. A dose response of multipolar mitotic spindles.	
MWCNT (D:10-20 nm L:1 µm) NanoLab, Inc. (Waltham, MA) SSA 200 – 400 m^2/g, 0.03% Fe and no content of Co and Ni	0.024-24 µg/ml for 24 h in BEAS-2B cells	Concentration-response of aneuploidy and polyploidy. The errors in chromosome number included more gains than chromosome losses. Concentration-response of disrupted mitotic spindle predominantly with a single pole	Siegrist et al. (2014)
MWCNTs (D: 5-20 nm, L: 0.3-2 µm) from a non-commercial source at Rostock University (Germany)	10 or 50 µg/ml for 24 h in human lung epithelial (A549) cells	Increased MN frequency (CBMN) at both concentrations (CBPI not reported)	Srivastava et al. (2011)
MWCNT (D: 10-30 nm, L: 1-2 µm, 95-98% pure) from Shenzhen Nanotech. Port Co., Ltd, China	1000 µg/ml in human lymphocytes (incubation time not specified)	Unaltered levels of MN frequency (CBMN) and sister chromatid exchange on samples from three different donors), with unaltered cell kinetics	Szendi & Varga (2008)
MWCNT (D: 10-30 nm, L: 5-20 µm, 15% impurities including iron)	*Salmonella typhimurium* TA102, TA1535 and TA1537	Unaltered mutation frequency	Taylor et al. (2014)
MWCNT, 6 different samples. NM400 (D: 11 nm, L: 0.7 µm, SSA: 280 m^2/g), NM401 (D: 63 nm, L: 3.4 µm, SSA: (300 m^2/g), NM402 (11 n, L: 1.1 µm, SSA: 250 m^2/g) and NM403 (D: 11 nm, L: 0.4 µm) from Joint Research Centre. NRCWE-006 (D: 69 nm, L: 44 µm, SSA: 24-28 m^2/g, from Mitsui & Co. Ltd Ibaraki, Japan) and NRCWE-007 from (D: 15 nm, L: 0.4 µm, SSA: 233 m^2/g, from Cheap Tubes Inc., Brattleboro, VT, USA)	2.5-250 µg/ml for 30 h in human lymphocytes	Increased frequency of micronuclei (CBMN assay) in all concentrations for NM403. NRCWE-006 was associated with increased micronuclei frequency at two low concentrations (2.5 and 15 µg/ml). NM402 was increased at one concentration (15 µg/ml), although it was regarded being an equivocal result. CBPI was unaltered at all concentrations	Tavares et al. (2014)
MWCNT (D: 6-24 nm, L: 2-5 µm, impurities: less than 0.4%) from Bayer	2.8-11.3 µg/ml for 24 h in human lung A549 cells	Unaltered MN frequency (CBMN, unaltered CBPI)	Thurnherr et al.

Table S-4. Micronucleus frequency, chromosome aberrations and mutations in cultured cells after exposure to carbon nanotubes (*in vitro* studies)

Material	Dose and cells	Effect	Reference
Technologies Service			(2011)
MWCNT (D: 15-30 nm, L: 10-20 µm) from own production as pristine or COOH-functionalized material	12.5 µm/ml for 1 h in A549 cells before a further 24 h incubation in medium with cytochalasin B	Increased MN frequency (CBMN, unaltered viability)	Visalli et al. (2015)
MWCNT (L: 0.2-1.0 µm, 5% impurities) from Bayer Material Science, Germany (Baytubes)	2.5-100 µg/ml for 4 h in Chinese lung fibroblasts (V79)	Unaltered levels of CA Unaltered mutation frequency in *Salmonella Typhimurium* TA 98, TA 100, TA 102, TA 1535 and TA 1537 with or without S9 mix	Wirnitzer et al. (2009)
MWCNT (D: 5-10 nm, L: 10-30 µm, 0.03% Fe, 0.02% Ni) from Nanostructured Amorphous Materials Inc	0.01-0.1 µg/ml for 24 h (co-exposure with cytochalasin B for CBMN test) in BEAS-2B cells	Increased MN frequency (CBPI not reported). Increased number of chromosome aberrations, especially related to genome amplification in a region of chromosome 2 that encodes a number of putative oncogenes	Wu et al. (2013)
MWCNT from Tsinghua and Nanfeng Chemical Group Cooperation, China (TEM pictures displayed individual tubes, although with possibility to estimate the length)	5 µg/ml for 4 h in mouse embryonic stem cells	Increased *Aprt* mutation frequency (2-fold compared to controls). Excluded from the review because of insufficient information about fiber characteristics	Zhu et al. (2007)

[a]Nanomaterial characteristics include tube diameter (D), length (L), specific surface area (SSA) and content of transition metals

CBMN, cytokinesis-block micronucleus assay; CBPI, cytokinesis-block proliferation index; SCE, sister chromatid exchange

Note: Micronucleus frequency induced by three samples of DWCNT was investigated in SHE cells and V79 fibroblasts exposed to 5 concentrations, 0.23-3.75 µg/cm^2 for 24h (Darne et al 2014). See note end of supplementary Table 2 for CNT characteristics. Two samples (DWCNT 2100 and DWCNT 2150) induced MN in V79 fibroblasts; DWCNT 2100: increased MN frequency at 2 concentrations (0.23; 0.94 µg/cm2), with decreased mitotic index, and DWCNT 2150: increased MN frequency at the lowest (0.23 µg/cm2) concentration, without alteration of the mitotic index at this concentration. No effect was found in SHE cells. DWCNT/DWEF increased MN frequency at the lowest concentration (0.23µg/cm^2) in SHE cells), and at the 2 concentrations (0.47; 0.94 µg/cm^2) in V79 fibroblasts.

Source: Adapted from Table 4 in Section 4.3 of IARC monograph 111 (IARC, in press), which was originally developed by authors on this paper. Table S-4 includes similar content but has been restructured alphabetically and several new studies have been added: Avti et al., 2013; Darne et al., 2014; Di Sotto et al., 2009; Jacobsen et al., 2008; Kim et al., 2015; Migliore et al., 2010; Mohiuddin et al., 2014; Mrakovcic et al., 2015; Nikitina et al., 2015; Ponti et al., 2013; Srivastava et al., 2011; Taylor et al., 2014; Wirnitzer et al., 2009; Wu et al., 2013; Zhu et al., 2007. Certain studies have been updated with information on mutations in mammalian cells and bacteria, which was not thoroughly covered in the IARC monograpm (Asakura et al., 2010; Ema et al., 2013a; Kim et al., 2011; Kisin et al., 2007; Manshian et al., 2013; Naya et al., 2011).

Section S-1. Route of Administration and Dose Metric

The intraperitoneal route of administration, as used by Rittinghausen et al. (2014) and others, is based on the intraperitoneal (or intrapleural) injection of fibers in liquid suspension at an European Union-recommended dose of 1 x 10^9 (or up to 5 x 10^9) of WHO fibers (JRC, 1999), which are defined as fibers >5 µm in length, < 3 µm in diameter, and having a 3:1 length:width aspect. Rittinghausen et al. (2014) selected a lower target dose of 1 x 10^8 WHO fibers per rat of amosite (asbestos positive control), based on the findings of Davis et al. (1991) that an intraperitoneal dose of 1 x 10^8 WHO amosite asbestos fibers per rat was associated with 50% incidence of mesothelioma two years after the intraperitoneal injection. The rat tumor response to the amosite control fiber used in Rittinghausen et al. (2014) was consistent with the approximately 50% tumor incidence expected based on the Davis et al. (1991) study.

The intraperitoneal route of exposure has been reported to be as predictive as the more costly chronic inhalation bioassays for cancer hazard evaluation (i.e., positive results seen for certain asbestos and man-made mineral fibers in animals dosed intraperitoneally or by inhalation). The intraperitoneal route was also shown to be specific for fiber carcinogenicity, as a total intraperitoneal dose of 80 mg of poorly-soluble particles was not carcinogenic in rats (Pott et al. 1991; SCOEL 2012) (compared to an intraperitoneal dose of approximately 1 mg of amosite asbestos being a carcinogenic in rats). However, the intraperitoneal route of exposure is typically not considered useful for risk assessment because of the limited information about the dose-response relationship (Rittinghausen et al., 2014).

An example of the challenge of quantifying the fiber number dose-response relationship is shown in Table S-5. The comparative potency of MWCNTs to asbestos depends on the dose metric. By mass, all MWCNTs appear to be more potent than amosite asbestos (i.e., similar or higher mesothelioma incidences of MWCNTs associated with lower mass intraperitoneal doses). However, on a fiber number basis, MWCNTs appear to be less potent than amosite (i.e., lower mesothelioma incidence per 1x10^8 MWCNT fiber dose than amosite). Oddly, higher intraperitoneal doses of MWCNT were found to have a lower mesothelioma incidence per 1x10^8 fiber dose (Table S-5). Davis et al. (1991) also observed an apparent inverse dose-response relationship in a study of amosite (Table S-6). This anomalous result may be due in part to increased agglomeration of fibers at the higher doses, which decreased the effective fiber number and surface area exposed to cells. In addition, there might be dose saturation, such that additional fibers do not cause additional tumor incidence. A high mortality rate due to a high fiber number dose would reduce the number of rats that develop cancer, which appear to lessen the influence of high doses on mesothelioma incidence. These studies illustrate the challenge of evaluating dose-

response relationships for mesothelioma. It is not clear what proportion of an inhaled dose of airborne CNTs and/or CNFs would reach the pleura in humans with occupational exposure. Estimated equivalent lung and pleural doses of CNTs in workers, based on limited available data, are described in Sections S-2 and S-3. Uncertainties associated with such estimates are discussed.

Table S-5. Intra-peritoneal (IP) administered dose of MWCNT in rats and mesothelioma incidence, including as estimated per 1x10^8 fibers (Rittinghaus et al., 2014).

MWCNT type and dose level	IP dose by mass or WHO fiber number		Mesothelioma Incidence (%)	Mesothelioma incidence (%) per 1x10^8 fibers[a]
	Mg	# fibers x 10^8		
A, low	0.2	4.8	98	20
A, high	1	23.9	90	3.8
B, low	0.6	9.6	92	9.6
B, high	3	48	90	1.9
C, low	0.08	8.7	84	9.7
C, high	0.4	43.6	94	2.2
D, low	0.05	15.1	40	2.6
D, high	0.25	75.4	70	0.93
Amosite	1.4	1.4	66	47
Vehicle Control	0	0	2	na

[a] Dose of 1x10^8 fibers per rat was associated with approximately 50% tumor incidence in the IP studies of amosite asbestos (Davis et al., 1991). na: not applicable

Source: Created for this paper based on data provided in the Rittinghausen et al. (2014) paper, and with new information on the mesothelioma potency (incidence per unit dose as fiber number).

Table S-6. Intra-peritoneal (IP) administered dose of amosite asbestos in rats and mesothelioma response, including as estimated per 1x10^8 fibers (Davis et al., 1991).

IP dose by mass or WHO fiber number		Mesothelioma Incidence (%)	Mesothelioma incidence (%) per 1x10^8 fibers
mg	# fibers x 10^8		
0.5	0.17	46.9	100 [a]
2.5	0.85	59.4	70
15	5.1	79.2	16

[a] Hit bound (100% maximum response).

Source: Created for this paper based on data provided in the Davis et al. (1991), and with new information on the mesothelioma potency (incidence per unit dose as fiber number).

Section S-2. Estimation of Human-Equivalent Exposure to a Rat Lung Dose Associated with Mesothelial Proliferation

Estimating the working lifetime equivalent airborne concentration to the rat lung dose that resulted in mesothelial proliferative lesions may provide some insight into the risk of precancerous changes at occupational exposures. It is also of interest to compare the rat lung doses associated with earlier biological effects with those cancer for the same material. A comparison of Tables 1 and 2 (cancer studies in rodents) shows little overlap in the specific type of CNT material studied to those in Table 6, which summarizes the shorter term studies in rodents exposed to various types of CNT or CNF. MWCNT-7 is the most studied (and only) CNT material to date with both early effects and cancer data.

Xu et al. (2012) reported that 1.25 mg of MWCNT-7 in rats (administered by intratracheal instillation at 0.25 mg/dose x 5 doses very other day) resulted in hyperplastic proliferative lesions in visceral mesothelioma. Thus, it is relevant to calculate the human equivalent concentration that would result in the equivalent deposited lung dose.

Extrapolation of lung dose from rat to human requires dose normalization to account for interspecies differences in the mass and/or surface area of the lungs. The lung weight (male F344 rat) was not reported in Xu et al. (2012). These estimates will assume 1 or 1.5 g, and for human lungs 1000 or 1200 g (ICRP 1994, 2002). The alveolar surface area assumed is 0.4 m^2 for rats and 102 m^2 for humans.

The rat total lung dose of 1.25 mg is either 0.83 or 1.25 mg/g lung (depending on the assumed rat lung weight). The human equivalent lung dose (mg) ranges form 833 to 1,500 mg (depending on the combination on the assumed rat and human lung weights). The human equivalent lung dose (mg) based on pulmonary surface area is lower at 318 mg.

The working lifetime equivalent concentration to result in the human-equivalent lung dose can be calculated as:

$$X\ mg/m^3 = Lung\ dose\ (mg) / (Air\ intake\ (m3/d) \times Total\ days\ exposed\ (d) \times Deposition\ fraction$$

where air intake is 9.6 m3/d (reference worker) (ICRP, 1994), the total days exposed is 11,250 d (250 d/yr x 45 yr), and the alveolar deposition fraction is assumed to be either 0.1 or 0.3.

The working lifetime concentration estimates (8-hr time-weighted average concentration) are 30 to 139 $\mu g/m^3$, assuming alveolar deposition fraction of 0.1; and 10 to 46 $\mu g/m^3$ assuming a deposition fraction of 0.3 (range of estimates reflects differences in the assumptions on lung weights or surface areas used in interspecies dose normalization). These occupational exposure estimates are based on the estimated total deposited pulmonary dose and do not account for difference in dose rate in rat and human or for clearance of some fraction of the deposited dose. These estimates suggest that some workplace exposures (Section 2.2) are in the range of these estimated human-equivalent exposures associated with mesothelial proliferation in rats. The margin of exposure to effect level is not very high for some of these estimates.

Section S-3. Estimation of Human-Equivalent Exposure to Intraperitoneal Doses of MWCNT in Rats

A key area of uncertainty is the relevance of intraperitoneal doses in rodents to human occupational exposure. To evaluate how rodent doses may relate to worker exposures, the working lifetime equivalent exposure to MWCNT was estimated as follows:

$$X\ mg/m^3 = Human\text{-}equivalent\ to\ Rat\ Intraperitoneal\ Dose\ (mg) / [9.6\ m^3/d \times 250\ d/yr \times 45\ yr \times 0.3 \times 0.02]$$

where the rat intraperitoneal dose is normalized by human body weight (e.g., 70 kg) to estimate the human-equivalent tissue dose, and there is an assumption of a 30% lung (alveolar) deposition of inhaled MWCNT, 2% translocation of deposited dose to the subpleural tissue (assuming no lung clearance), and worker air intake of 9.6 m^3/8-hr/d, 250 workdays per year over a 45-yr working lifetime. The alveolar deposition of 30% is based on

Ryman-Rasmussen et al. (2009), although other estimates of airborne CNT alveolar deposition fraction are closer to 10% based on the Multiple-Path Particle Dosimetry (MPPD) model (NIOSH 2013; ARA 2009). The 2% translocation is taken from Mercer et al. (2011), who reported that 1.6% of a MWCNT administered dose (80 µg) was measured in the subpleural tissue on day 56 post-exposure. Subpleural tissue is defined as "the region consisting of the mesothelial cells of the visceral pleura and immediately adjacent interstitium" (Mercer et al. 2011). In these estimates (Table S-7), any CNT that reaches the subpleural region is assumed to be able to reach the pleura. The worker-equivalent airborne concentration estimates in the range of 0.013 to 13 mg/m^3 over a 45-year working lifetime are estimated to be an equivalent pleural dose to the intraperitoneal doses in the rodent studies, assuming no clearance of CNT inhaled and deposited in the lungs and an aveolar deposition fraction of 30%. The widdest range of doses per kg body weight are in the Takagi et al. (2008, 2012) studies; the doses in the other studies are within that range (Table S-7). While it is unlikely that workers would be exposed to either MWCNT or asbestos at those concentrations, such exposures are similar to the permissible occupational exposures for other carbonaceous, poorly-soluble respirable particles (e.g., 1-5 mg/m^3 for coal mine dust, carbon black, or particles not otherwise regulated) in the U.S. (NIOSH 2007) and other countries.

Rittinghausen et al. (2014) reported a mesothelioma incidence of 40% in rats administered with the lowest IP dose in that study of 0.05 mg (MWCNT “D”); the estimated human-equivalent working lifetime exposure concentration was 18 µg/m^3 (calculated as shown above in this section) (Table S-7). In Takagi et al. (2012), a mesothelioma incidence of 25% was reported at the lowest IP dose of in that study of 0.003 mg (MWCNT-7); the estimated human-equivalent working lifetime exposure concentration was 13 µg/m^3 (Table S-7). Although the dose rate of MWCNT over a working lifetime assumed in these estimates is considerably less than that in the IP studies, the estimated equivalent working lifetime exposure concentration is relatively low and in the range of airborne exposures of inhalable or respirable size MWCNT in the workplace (Section 2.2).

Uncertainties in these human-equivalent exposure estimates include the following:

1. Pulmonary clearance (alveolar macrophage-mediated) is not taken into account in these total deposited dose estimates. This would tend towards overestimating the working lifetime retained lung dose.

2. There is uncertainty in the estimate of 2% of the lung deposited dose translocating to the subpleural tissue (in mice at 56 days) to humans over a 45-year working lifetime. The tendency here may be toward underestimating the portion of the deposited dose that reaches the subpleural tissue over a working lifetime.

3. Rather than an alveolar deposition fraction of 0.3, an estimate of 0.1 is more consistent with airborne particle sizes used in the rodent inhalation studies. If a 0.1 alveolar deposition fraction is used, the human equivalent concentrations would be approx. 0.039-39 mg/m^3.

4. Questions arise about comparability/equivalency of the site of human mesothelioma versus the intra-pleural or intra-peritoneal tissue sites in the rat experimental studies.

Table S-7. Rough estimates of human-equivalent exposure concentration over 45-yr working lifetime to reach an equivalent subpleural dose as used in rat intraperitoneal studies, based on available data and assumptions as described.

CNT type	Study	Species, strain, gender	Rodent IP dose, as reported (in Table 1)	Rodent IP dose (mg/kg BW)	Human-equivalent dose (mg/70 kg)	Working lifetime exposure concentration (mg/m^3)[c]
MWCNT (ground)	Muller et al. (2009)	Rat, Sprague-Dawley, male[a]	2 or 20 mg MWCNT	4	280	0.43
				40	2,800	4.3
			2 mg crocidolite	4	280	0.43
MWCNT-NT50	Nagai et al. (2013)	Rat, F344-Brown Norway F1 hybrid, male and female[b]	1 or 10 mg	3	233	0.36
				33	2,333	3.6
MWCNT (various types)	Rittinghausen et al. (2014)	Rat, Wistar, male[b]	0.05 to 3 mg	0.17	11.7	0.018
				10	700	1.1
MWCNT-7	Takagi et al. (2008, 2012)	Mouse, C57BL/6, male[d]	0.003 to 3 mg	0.12	8.4	0.013
				120	8,400	13

[a] Body weight approximately 0.5 kg.
[b] No rat body weight (BW) reported; assume 0.3 kg.
[c] Assumptions: 70 kg human, 30% lung (alveolar) deposition of inhaled MWCNT, 2% translocation of deposited lung dose to the subpleural tissue (assuming no lung clearance); worker air intake 9.6 m^3/8-hr d; 250 workdays per year.
[d] Assumed mouse BW of 0.025 kg.

Source: Created for this paper based on information on dose in the studies cited, with new information from calculations of the normalized IP dose in rodents and the human-equivalent dose and working lifetime exposure concentration.

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