SUPPLEMENTAL INFORMATION

Size dependent deposition of inhaled nanoparticles in the rat respiratory tract using a new nose-only exposure system

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TABLE S1
Iridium-192 sample counting detection efficiencies

Counter	Organ	Detection efficiency*
Wizard	Head Pelt	0.53 ± 0.04
Wizard	Kidneys, Spleen, Blood, Lung Lobes	0.61 ± 0.05
Wizard	Liver	0.58 ± 0.04
Well	Any Organ	0.70 ± 0.02

*Detection efficiencies, including the effect of sample geometry, were determined using a number of iridium-192 'check' sources, including a small iridium wire source irradiated at the imperial College Reactor Centre (Ascot, UK) and some produced in-house by depositing iridium-192 aerosol particles onto 47 mm Pallflex filters (EMfab TX40H120-WW, PALL Life Sciences, Ann Arbor, MI, USA). These sources were counted using a custom-built Hyperpure Ge detector system (Canberra Industries Inc., CT, USA) operated in compliance with ISO/IEC 17025:2005, to determine their iridium-192 activity. The Well Counter detection efficiency was found to be largely invariant (<0.5%) with regard to check source geometry, however, the detection efficiency of the Wizard counter did vary noticeably with source geometry due to its smaller crystal size. For the Wizard counter, sample type specific detection efficiencies were determined by positioning the small iridium-192 source at various points within a counting vial. This approach was checked by measuring some samples in both the Well and Wizard counters, and good agreement was found.

TABLE S2
Rat respiratory tract and breathing parameters used in MPPD v2.11

Parameter (unit)	MPPD v2.11 default	Experiment Specific*
FRC (ml)	4.0	3.7
URT volume (ml)	0.42	0.29
Breathing frequency (/min)	102	127
Tidal volume (ml)	2.1	1.3

*FRC volume from Filho et al (2014), URT volume derived by body mass scaling according to Menache et al (1997), other values experimentally determined.

TABLE S3
Iridium-192 content of organs and tissues at 24 hours

Nominal aerosol particle size (nm)	Iridium-192 content (Bq)			
	Lung	GIT	Head	Remainder
10	4370 ± 550	893 ± 318	20.1 ± 9.4	10.4 ± 3.7
15	8195 ± 1729	735 ± 362	10.1 ± 4.0	112 ± 142
35	3932 ± 416	158 ± 110	1.8 ± 0.6	10.5 ± 15.8

TABLE S4
Predicted deposition fractions (MPPD v2.11) for default and experiment specific breathing parameters

Particle diameter (nm)	Deposition Fractions									
	Respiratory Tract		Alveolar		TB		Lung*		Head	
	Default	Specific	Default	Specific	Default	Specific	Default	Specific	Default	Specific
9.8	0.749	0.715	0.221	0.165	0.174	0.167	0.395	0.332	0.353	0.384
15.6	0.547	0.495	0.278	0.210	0.094	0.092	0.372	0.302	0.176	0.193
35.2	0.361	0.313	0.219	0.163	0.049	0.048	0.268	0.211	0.093	0.101
76.3	0.236	0.205	0.149	0.113	0.029	0.030	0.178	0.143	0.058	0.062

*Sum of alveolar and TB

FIGURE S1. Cross-sectional view of exposure chamber indicating flow-splitting cone (EMMS, Bordon, UK).

(a)

(b)

FIGURE S2. Variation in aerosol delivered across all ports of exposure manifold. Mobility equivalent particle size distributions and particle number concentrations were measured at each of the 36 ports in the exposure manifold using an SMPS. Two size distribution scans were done for each port and the order in which ports were sampled from was randomised across the four chambers in order to minimise the effect of any temporal variation in the size distribution. For each port, the average of the two size distribution measurements was taken and for each chamber the average and standard deviation of all measurements made at its 9 ports were generated. This was carried out for all particle sizes investigated in this study. For all sizes, the number concentration, count median diameter (CMD) and geometric standard deviation (GSD) measured at any given port did not vary by greater than $\pm 4\%$ from the chamber or manifold average: (a) example of the percentage variation in number concentration, CMD and GSD measured at each of the 9 ports from the chamber average for one chamber (chamber 2); and (b) average size distribution for each chamber for the nominal 15 nm aerosol (error bars shown are the standard deviation).

FIGURE S3. Representative TEM images of nominal (a) 10 nm, (b) 15 nm, (c) 35 nm and (d) 75 nm iridium-192 aerosol particles. All images are at 80000X magnification.

FIGURE S4. Representative example of a high magnification (400000X) TEM image of an iridium-192 agglomerate illustrating the crystalline structure of the primary particles. Particle agglomerates of all sizes displayed the same primary particle size and crystalline structure.

FIGURE S5. Example EDX spectra of Iridium agglomerate particle taken with a nominal 5 nm probe. Only iridium could be detected in the particles (note: the copper signal originates from the TEM grid).

FIGURE S6. Specific activities of lung lobes at 0 h and 24 h, for 15 nm aerosol, indicating uniformity of distribution (note that lungs were fixed for storage prior to dissection of lobes and thus lobe weights may differ from initial wet tissue weights).

FIGURE S7. Experimentally derived deposition efficiencies in the respiratory tract (A), lung (B), head airways (C) and alveolar region (D) determined using breathing rate from Filho et al (2014), and MPPD v2.11 model predictions using default respiratory parameter values (solid line) and experiment specific values determined assuming breathing rate from Filho et al (2014) (dotted line). Note that the model predictions are very similar for the two sets of input data, especially for the

respiratory tract and head airways for which the two plots are essentially coexistent. Note also that for the lung and head airways two experimentally derived values are presented. For the lung: (●) values derived using iridium-192 content of lung only, and (▪) values derived using the sum of the iridium-192 content of the lung, GIT and other organs and tissues (i.e. assuming iridium-192 in the GIT and other organs and tissues was originally deposited in the lung). For the head airways: (●) values derived using iridium-192 content of head airways only, and (▪) values derived using the sum of the iridium-192 content of the head airways and GIT (i.e. assuming iridium-192 in the GIT was originally deposited in the airways). In both cases (●) is an underestimate and (▪) an overestimate with the expected value lying between.